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THE JOURNAL OF PEDIATRICS

A MONTHLY JOURNAL DEVOTED TO THE PROBLEMS AND DISEASES OF INFANCY AND CHILDHOOD

BORDEN S. VEEDER
St. Louis
Editor

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A DROPPER FULL OF COMFORT

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Original Communications

CHANGING MEDICAL CARE IN OUR CHANGING NATIONAL LIFE

EDWARDS A. PARK, M.D.

BALTIMORE, MD.

SINCE I am addressing the pediatric section of the Academy, my audience may expect me to dwell on the social problems related to the care of children. But the care of children is just a part of the medical care problem of the population in general, and cannot be separated, although attempts were proposed in the Pepper Bill and in the minority report No. 1 of the New York Legislative Commission on Medical Care. Accordingly, I shall treat the topic in its general aspects. But before beginning, I must make an explanation: I shall speak as if the medical care problem pertained only to physicians, hospitals, medical schools, and the people, although I realize as much as anyone that it concerns also dentists, public health workers, nurses, social workers, laboratory workers, and all others whose duties are concerned with the maintenance of health and the problems of disease. I include the *people* with all the emphasis I possess, because the general policies under which public funds are expended must be developed fully in the interest of those who are to be served, the consumers of the medical care. Although, by universal admission, the sole authority in all matters pertaining to the applied science and art of medicine is the physician, in the economic aspect of medical care and, to a considerable extent, in the administrative, the consumers, i.e., the people themselves, have equal rights and are equally concerned with the physicians. How much medical care will cost, how it will be paid for, in what form it will be offered, and just how it will be carried out, these are matters vital to the people also. So, on every administrative board which decides or administers medical care plans at every level, federal, state, or local, the receivers of medical care, the people, must be adequately represented, together with the professional groups, the givers. I say this because I think that many physicians feel that they are the sole authorities, the only ones who really know what is best, and that the people should meekly receive what they decide to give. They forget that physicians are a vested interest and are instruments, not ends, and that selfish hopes and wishes loom large so as to blot out parts of

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the perspective or hide the view altogether, and cause them unconsciously to think of how to safeguard personal comfort and profit rather than of the best interests of the people whom they serve.

If I remember correctly, in the brief time when the present Duke of Windsor was King of England, he visited the slums to see with his own eyes the housing conditions, and on that occasion made a profound remark which evoked great praise in the British press. The remark was: "Something must be done about it." I think we are all convinced that something must be done about the present state of medical care, but what form that *something* should take and how that *something* should be put into effect have stirred up great conflicts of opinion.

Why is it so necessary to change the present system of medical care? The present system has developed spontaneously to fit the distribution of money, not the distribution of medical need; it does not meet the medical need and, no matter how it might be extended, could never meet the medical need in one thousand years, for the reason that it operates on an incorrect principle. Another reason is that its fee-for-service system of remuneration keeps it from taking on a preventive character because the person who pays a fee to his physician at each visit goes to him only when sick. Another reason is that the science of medicine has developed with such strides that the requirements of medical care have changed, and groups of minds must now collaborate, since single minds can no longer be masters of more than small parts of medical knowledge. Moreover, as in industry, laboratories and machines of great complexity have become essential. As the result of all this, the family physician who was once so adequate can no longer meet all necessary services by himself. He and his patients must have available specialists, x-ray service, laboratories. This transformation of medical care into something far more complex and beneficial has, unfortunately, so increased its cost that it has risen out of reach of the majority of people. Without presenting the evidence, it is sufficient to say that the present happy-go-lucky, haphazard system of medical care has become outmoded and out of joint and is hopelessly insufficient and inadequate to meet the health requirements of the nation. This is one side of the picture. The other is that the great advances in science and industry have made possible higher standards of living. Moreover, the methods of science have been employed as never before in economics and sociology, with the result that the facts of living, including health, have been studied and are intimately known. The knowledge thus gained has brought to pass a greatly intensified social consciousness and feeling of social responsibility, in brief, has led to an intensification of democracy in the finest sense of the word, meaning, thereby, the general acceptance of the principle that individuals have equal rights to fair shares of the comfort and benefits of life. Finally, large groups of the population, labor and farm groups in particular, have awakened to the idea that a new kind of medicine has come into being, and on all sides we see them organizing in the attempt to secure it. As a boy, I once heard President McKinley say in a campaign speech that he kept his ear close to the ground so that he could hear the voice of the American people. In reality, I suspect he kept it about five feet, four inches from the ground so

that he would not miss a word from Mark Hanna. But, however that may have been, the legislators have now sensed what the people want, and that is the significance of President Roosevelt's inclusion in his "second Bill of Rights," "The right to adequate medical care and the opportunity to achieve and enjoy good health," and the Wagner-Murray-Dingell Bills, the first introduced in 1943, and the ancillary Pepper Bill, and the more recent Taft-Smith-Ball-Donnell Bill, represent attempts to realize this objective practically. To my mind, President Roosevelt's inclusion in his "second Bill of Rights," Jan. 11, 1944, of the idea that each citizen had a right to the best medical care quite apart from his financial position, is a landmark in the medical history of the country, for the concept is so just, altogether right, and feasible, fills so burning a need, and was given such prominence through iteration by the late President, that there can be no going back. Every plan for medical care since the enunciation of this principle has perforce been aimed, on the surface at least, toward that magnificent goal.

The general objectives in a Utopian medical care program are easy to see but difficult to reach. There must be an adequate number of splendidly educated physicians. An educational system must be set up to keep the physicians of the nation abreast of medical progress. New hospitals and centers of different sizes and functional scope must be dotted over the country according to community needs, and they must be serviced by groups of specialists and must be equipped with laboratories and all the latest machinery of medicine. The study of disease and its prevention must be fostered and extended constantly. Finally, the physicians themselves must be well paid, and their lives and work made attractive, in order to bring into the profession, which is entrusted with the health of the nation, the best talent possessed. These objectives or principles are at the basis of medical programs in the more socially-minded countries and the programs differ chiefly only in the degree of centralization and rigidity with which they are organized. I shall speak of these principles presently.

In this country, there are great obstacles in the way of realizing the objectives just mentioned. The physical parts of the program, that is, the construction of hospitals and centers, is the easiest part. It will not be difficult for the medical schools, if given facilities and if prodded a little, to turn out more and better educated physicians. The experience in England and in New Zealand has shown that it is not so hard to give the population-at-large general practitioner service. The great obstacle—and it is enormously great—is psychological and lies in making physicians and the people, accustomed over years of habit to do something one way, to do it another. It would probably not be so difficult to change the habits of society; the great difficulty is in changing the habits and points of view of the medical profession, that is, in uprooting and changing over a system of medical care which is the outgrowth of centuries.

Another difficulty of a very practical nature in effecting changes in medical care, is that in the profession of medicine itself there is no leadership. I shall come back to this subject later.

In the main, there are two divisions of thought in planning a system of medical care which will suffice to meet the health needs of everyone; one is

that a new complete system, covering all the medical care needs of the entire population from "the cradle to the grave" ought to be imposed all at once, and the other, that it is wiser to proceed gradually. Those in favor of the more radical, drastic course are the supporters of the Wagner-Murray-Dingell Bill, S.1606, 1945. I shall not discuss this bill, but merely express the opinion that, if it were passed tomorrow, medical care would be thrown into unbelievable chaos, for the reason that we are not prepared for its sweeping changes. We lack the physicians, hospitals, organization, and the appropriate psychological attitude of the profession necessary for success, and I do not believe that the people of the country are psychologically prepared for the change. The enactment of the bill now would result in a debacle such as would have occurred if the invasion of Normandy had been attempted at the outset of the war without the necessary troops, training, transport, or equipment. Starting from scratch today, it would take fifteen years to become completely ready to meet the requirements of the bill. The dangers and difficulties of imposing revolutionary programs of medical care on an unprepared and inadequate medical organization are illustrated by the experiences in New Zealand, which I shall discuss later. Before leaving the Wagner-Murray-Dingell Bill, however, I wish to point out that the bill itself is open to serious criticism. For one thing, it is altogether too highly centralized and rigid. On the other hand, it has great merits: it represents a splendid attempt to work out a medical care program clearly and logically. Its completeness has made it a huge target. It is the product of a fine idealism, and it has had a magnificent influence in that it has made both the people and physicians think, and, in the case of organized medicine, fear and stir a little, for it has been handwriting on the wall. Finally, I express the opinion that in the end the form which medical care will take in this country will not be so far removed from the one outlined in the Wagner-Murray-Dingell Bill, but more decentralized and flexible. I say this because in the medically progressive countries of the world, the systems of medical care either in operation or projected are of that same pattern, and that pattern seems to be the one toward which the development of medical care is moving the world over.

The second division of thought, holding that it is wise for us to proceed slowly in the development of a medical care program, is supported by the great majority of physicians. The general thought underlying this view has just been expressed admirably by President A. E. Morgan of Antioch College (*Antioch Notes*, Feb. 14, 1947), "Social change should combine planning and improvising. We can tentatively plan limited phases of our common life, then, watching the effects and taking into account factors first overlooked, we can replan and revise. By this step-by-step process, more than by a grand sweep of theoretical planning, will come a new society." I, too, hold this view, but I am fully aware of the dangers inherent in the policy of trusting to a step-by-step process, and have no sympathy with the attitude of many of my medical friends who believe in doing nothing and trusting to "evolution," meaning thereby really doing nothing themselves to guide change but leaving the guiding to other people—lay groups, theorists, and politicians. Evolution means change through the dying

out of the unworkable and the survival of the workable. Evolution in this sense goes on all the time no matter what we do and determines or undoes, in the end, the work of mice and men. But it is a very slow, merciless, wasteful process, and now there is no time to delay, for the public will take matters in their own hands through the agency of the government as they have done in England and New Zealand. Witness California at the moment!

But there are excellent reasons for going slowly, if we can only use them. Would it not be foolish to pass such a bill as the Wagner-Murray-Dingell Bill without waiting to see how the National Health Service Bill works out in Great Britain in the first year or two? We have before us the examples of Canada and New Zealand, the former setting a splendid precedent and the latter showing something to avoid. Then there are the Swedish and Russian systems, which I should like to discuss now.

The Swedish system of medicine is a combination of State and private practice systems. There is a voluntary insurance system, which, by 1944, had spread to 42 per cent of the population, but a large number of those who were poorest financially were still not members. Because the voluntary system has not reached the lowest income groups, and because it has been so successful in the case of the others, the government is about to make the insurance system compulsory. The medical students are of the elite of the preparatory schools and the general medical education equal to that anywhere in the United States. Hospitals and centers are distributed so as to be available to all, as are complete medical services, including those of the specialists. I now quote from a letter from Professor A. Lichtenstein (J. PEDIAT. **28**: 503, 1946):

"As can be seen from this account, we have in Sweden a combined system of State and private medical care. The State and the municipality, partly with the help of the sick relief funds, ensure that every sick person, irrespective of his financial situation, has the opportunity of obtaining the best possible medical care either in the hospital or outside. To this end, the best specialists in the country in various fields are available as salaried medical officers at hospitals and as doctors for outpatients. The patient has, to a great extent a free choice of physician. *In my opinion, the free choice of a physician is necessary, for the patient, and for the physician, even in the case of members of sick relief funds, which embrace the largest proportion of the country's population.* The medical profession in Sweden is free, so that the individual doctor can, within a wide boundary, of his own free will choose the place and type of his activities. Even doctors appointed by the State or the municipalities are entitled, in so far as their work at the hospital permits, to carry on their profession with complete freedom.

"This system has, in my experience, functioned well, and on the whole fulfills the wishes of both the patient and the doctor. It is my opinion that a substantial state subsidy and control is necessary if the health and care of the sick in a country are to function effectively and satisfactorily. The fears expressed by some doctors, that a state activity as regards medical care would hamper or prevent the practicing doctor's exercise of his profession, have proved themselves to be unjustified. On the contrary, the work, for example, of the

child welfare centers has increased the interest of the public in child welfare and the care of sick children, and private pediatricians are sought in an ever-increasing degree. Such a development, however, presupposes that the state medical activities are not so organized as to make private medical practice impossible. *I fear that should medical activities be entirely controlled by the State, this would, in all certainty, lead to an unfortunate medical bureaucracy and also to an elimination of the personal contact between the patient and the doctor, which is a necessary condition for all good medical activity.* Such a socialization would mean, for the medical profession, a lowering of the standard which is in direct opposition to the interests of the country. *The duty of the State is, however, to organize medical care in such a manner that every person, irrespective of his income, can procure the best preventive and curative medical care.*

"In my opinion, the Swedish system shows very clearly that this can be done without undermining private medical practice."

Sweden has only 6,500,000 inhabitants (1945) and a geographical area smaller than France, and its population is homogeneous, disciplined, and organized. The problem there was simple as compared to ours. Their system is the result of an indigenous growth and cannot be copied, but it demonstrates that it is untrue and therefore sheer nonsense to think that State medicine and private practice systems cannot get on together successfully and happily or that State medicine need interfere with the free choice of physician or patient or with the physician-patient relationship. Moreover, it shows that through State planning and intervention, medical service can be made available to all the lower income groups, not just general practitioner but comprehensive medical care. Finally, the system is approved by the physicians themselves. Professor Wallgren (J. PEDIAT. 30: 361, 1947) states that, in general, the physicians choose State positions in preference to private practice because of their greater security. I ought to add that in the development of the medical care plan in Sweden organized medicine has played a great part, and with its almost dictatorial power, is instrumental and, perhaps, the main force in keeping the State system at its high efficiency. I believe that if our medical care system equalled Sweden's we would have no medical care problem.

The trouble with evaluating the Russian system is that, though we know it on paper, we do not know it in operation. On paper there are excellent features: One is that there is a highly developed screening process in the education system designed to insure that the physician class have exceptional ability, and there is further screening in order to separate out the most able for the superior medical positions. Another is that the state makes special provision for the continued education of the practicing physicians throughout their active lives. A third is that the State pays the expenses of the medical student during the years of preparation, so that medical education is open at all economic levels. So far as pregnant women and children are concerned, the health program is, perhaps, the most inclusive to be found anywhere. Of course, the system is rigid and centralized, but the test is what it does for the health of the people, and that I do not know.

If we accuse Russia of imposing an iron curtain, we cover our eyes when we look toward Russia with the blinding veil of prejudice. I suspect there is much to be learned from the medical care system of Russia, and it is stupid to assume that it offers nothing to us, just because we do not like the cut of Russia's ideology. We must beware that in twenty years' time we are not outdistanced by that young, new-thinking nation, in terms of what a medical system does for the health and security of the people. Dr. Mudd's report, in *Science* (*Science* **105**: 269, 306, 1947) reveals the biological laboratories of Russia teeming with activities and ideas.

Then we have our own experiments in medical care—those in progress in Maryland, North Carolina, Washington, D. C., and New York City, as well as many others scattered over all parts of the country, some started by physicians and some by lay groups. The hope and probability is that one or two of these experiments will emerge as unusually successful and serve as models. Unfortunately, I have not time to discuss these, but their spontaneous birth in so many places in so short a time is a portentous, healthful, promising sign.

A most important step, and by general agreement, one wholly in the right direction, is the Hospital Survey and Construction Act (the Hill-Burton Act), which is intended to furnish the physical setup for the extension of medical care to the areas of the country where most required. Its general features are excellent. The State survey is essential. The provision that the State can make its own plans, based on its survey, is admirable, and the limitation of the Federal role essentially to standards and guidance is as it should be. Under it, the states have the desirable autonomy, and yet the federal government has enough power to make certain of a carefully integrated and coordinate state and national plan. In brief, the balance between state control and federal control seems just and right. Then, also, it is a happy arrangement that the United States Public Health Service has the administrative assignment, for that splendid agency possesses uniquely the knowledge, organization, and high ethical standards required for this particular purpose. I know from experience that the United States Public Health Service can be of the greatest help in furnishing hospital plans. Finally, the establishment of the hospitals and centers is an absolute requirement if the very latest developments in medicine are to be made available to all the people in the country.

But the Hill-Burton Act has some rather glaring deficiencies. It has no provision for federal funds to aid in the maintenance of the hospitals, once they are constructed, and it has the same matching requirement for the poor and the rich states. This last means that the areas of the greatest need, the more rural states and communities, and those with less wealth which should profit the most are in actuality, discriminated against. While the federal funds are allotted to the states in such manner that the poorer states may receive larger proportions of the amounts available, the result of requirement for uniform matching is that the poorer states are less able to take advantage of the federal offers. Thus, no real equalization has occurred.

Bill S. 545, introduced by Senators Taft, Smith, Ball, and Donnell, I shall refer to as the Taft Bill. It is at the opposite extreme from the Wagner-Murray-

Dingell Bill and is obviously written to appeal particularly to those to whom Federal control is anathema. The Taft Bill vests essentially all the authority in the individual states and reduces the Federal control nearly to impotence. If the Wagner-Murray-Dingell Bill was carefully thought through and made to face issues squarely, the Taft Bill is poorly thought out and avoids controversial issues, except for its central thesis of states rights, by passing them on to be fought out in the individual states. It contains provisions fraught with peril. For example, the Bill provides that "no plan or modification shall be disapproved because the (Federal) Director disapproves of the methods proposed." This would probably be interpreted as prohibiting the establishment of Federal standards which a state would have to meet in order to have its program approved. Virtually all of the existing health legislation requires the establishment and maintenance of personnel standards on a merit basis. Such Federal legislation has been a most important factor in taking politics out of health department appointments. Such a merit system clause was in the original Taft Bill introduced last year, but its omission is conspicuous in the present bill. The removal of this would open the State programs to political appointments. Proposals in the bill would allow the State to purchase services through any nonprofit, voluntary insurance program without any standards whatsoever. This would permit state and federal funds to be used to subsidize poorly operated voluntary insurance programs. Moreover, within the National Health Agency, seven units are established, one of which is the new Office of Medical and Hospital Care Services. This unit is administrated entirely separate from the United States Public Health Service and the Children's Bureau, i.e., the existing federal health agencies have been completely by-passed. This arrangement creates obstacles in the way of integrating preventive health services and curative health services. If the Bill were passed as it stands, there could be as many different systems of medical care as there are states. Some of these in the more progressive states would probably be very good, in some other states exceedingly poor, and all would be laid open to the possibility of political intrigue and inefficiency. If the passage of the Wagner-Murray-Dingell Bill would produce chaos in medical care, the Taft Bill would produce national confusion and perhaps corruption, and would establish an inefficiency which it might be impossible to overcome. It would span the way to the perpetuation and extension of the poor features of the present system of medical care without the assurance of new good features. The bill has other questionable provisions, one of which, having to do with a proposed extension of voluntary insurance to the medically indigent groups, I discuss later. But the bill is an example of careless thinking, or not thinking at all, and the fact that such a manifestly inferior measure could be proposed by our legislators is depressing to those who perceive how glorious a medical care program might be.

If it is wrong to give all the power in health legislation to the Federal Government, it is worse to place it all in the States and to have no national integration or coordination. In determining Federal and State relationships there must be a happy medium, in which the Federal Government establishes the general scheme and fixes minimum standards and the States have freedom to

develop their own systems within the Federal structure. The plan for compulsory health insurance which the Canadian Medical Association has recommended to the Canadian government is in marked contrast to the Taft Bill in the wisdom with which the Federal-Provincial relationship is arranged. Their recommendation (The Medical Profession and Health Insurance: a Submission to the Special Committee on Social Security of the House of Commons by the Canadian Medical Association, 1943, J. PEDIAT. **31**: 228, 1947) reads: "If Provincial autonomy is to be maintained as suggested above, it is extremely important that a sufficient degree of federal control be retained. This control should be limited to such matters as the extent and the standards of the services, as indicated previously. It is important, however, that control be maintained as it is only through this means that a satisfactory degree of uniformity can be obtained. Unless there is considerable similarity in methods and program in matters of disease prevention and control, the results from the national viewpoint will be jeopardized. . . .

"On this basis it is recommended that the federal administration be under the Minister of National Health, with an Advisory Dominion Council on Health Insurance.

". . . in the provinces it is strongly recommended that the plan come under a *non-political independent commission* which might be responsible to the legislature through the Provincial Minister of Health. . . ."

Among the details left to the Provinces might be "the income level . . . below which the residents would be included under an obligatory plan; the rate and method of payment for all services, professional and institutional; the best means of obtaining full preventive and public health services within the Province concerned; and the particular means which might be necessary to safeguard the basic necessity of maintaining adequate teaching services in connection with Medical Faculties and Teaching Hospitals within the Province."

The Taft Bill contains a suggestion that voluntary insurance be extended to the medically indigent through the use of tax money to pay the cost of coverage in voluntary prepayment plans. This raises the topic of insurance under public auspices, supplemented, as necessary, from general tax revenues. This is probably the best method for financing complete coverage for medical care for the entire population of the nation. Its merits, as an immediate measure, will be discussed by Dr. Ernst Boas in the April number of the JOURNAL OF PEDIATRICS (**30**: 478, 1947). As just stated, the Canadian Medical Association recommended, in 1943, to the Canadian Government, a compulsory health insurance system which could be made to include everybody or only those in certain income levels, according to the determination of each province. I do not believe that we in this country are yet prepared for universal health insurance, either psychologically or materially. The enactment of universal health insurance without an intervening period of planning, would throw the full weight of providing necessary care for the entire nation upon our present limited resources before they have been built up to the required strength. If, however, a Federal-State health insurance scheme, supplemented from general taxes when necessary, were made available to the low and middle income groups, the burden

on the physicians and medical care resources of the country would still be great, but, perhaps, not too great, if time were granted for gradual adjustment.

Voluntary insurance has been taken up by the public like wildfire. The Blue Cross has now 24,250,000 subscribers, one-fifth of the population of the country, and prepayment medical care schemes such as those offered by medical and consumer groups have been extended considerably. But practically all voluntary insurance plans supply only partial medical care and that for only a limited period of time, in the sense that they cover only catastrophic illness and they do not provide for preventive medical care. These deficiencies are tremendous and keep the present plans far from meeting the total need of even those financially able to subscribe to them. Moreover, the plans are circumscribed by specific factors, such as occupation, economic status, residence, race. Nevertheless, the voluntary hospital insurance plans have been a great benefit, and their popularity indicates that the prepayment principle is generally desired. My medical friends who favor a hands-off waiting policy in regard to the development of medical care, and they are many, say to let voluntary insurance spread until it reaches everyone who needs it. But it is obvious that voluntary insurance can never spread to those who need it most, namely, to the low income groups, for they can never afford it. Furthermore, experience shows that plans offering complete medical coverage are necessarily too costly for most families, even those in the middle income groups. This accounts for the slow growth of voluntary medical service plans.

Returning now to the Taft Bill, it suggests undertaking to provide care for medically indigent persons through payment of insurance premiums with tax monies to all types of nonprofit voluntary plans. This would appear to be a policy based on fallacious reasoning, since it would involve inappropriate use of public money and would be unsound governmental procedure. It is a long-established principle that tax money should be expended by public agencies which are accountable to public officials representing the tax payers. This is a basic principle in the organization of our government, and hence a vital consideration against the Taft Bill proposal, aside from the fact, as I have pointed out above, that voluntary plans do not generally assume responsibility for meeting more than the very partial medical needs of their members. It seems astonishing that Senator Taft and his associates should have allowed a suggestion flaunting this time-honored principle to be introduced into the bill.

In any prepaid medical care program in which the care offered is to cover all requirements, the method of compensation of physicians is of great importance, and since our present medical care system is founded on a sliding fee-for-service remuneration, I shall briefly discuss the fee-for-service method of reimbursement and give the experiences with it reported from New Zealand. The fee-for-service method of payment of physicians has the great merit of stimulating competition, and this is its virtue. However, it has serious drawbacks: Most important, it stands in the way of preventive medical care, for the obvious reason, as previously mentioned, that, if a person has to pay a physician for his visit, he will not go to him until sick. The method interferes more than anything else with the naturalness of the patient-physician relationship. It is

not democratic, for it creates economic and social distinctions. High-priced physicians in the main have rich patients and low-priced physicians the poor, and the low-priced physicians in consequence are the ones who carry the great burden of charity and are not so well equipped to do first quality work in consequence of heavier load and poorer facilities. Moreover, the method of payment stimulates avariciousness and breeds fee splitting. In short, it is the chief cause of criticism or of actual charges against the medical profession. Finally, as previously pointed out, it gives a wholly wrong distribution of medical care. When it is introduced into a prepaid complete coverage medical care plan or one based on direct payment by the State for service rendered, it is difficult to control and is likely to wreck the system. The New Zealand experiment in medical care illustrates the difficulties caused by the fee-for-service variety of payment.

The New Zealand plan, in brief, is that the government provides medical care for everyone by paying for medical and pharmaceutical benefits according to fixed rates. The fee-for-service or "direct claim" system was intended by the government to be the standard and has been the one chiefly used, though capitation and salary reimbursement have been employed to some extent. Under the fee-for-service system, the patient signs a form stating that service has been rendered and the physician sends in the form to the health department and receives 7s, 6d per service. This is the ordinary arrangement, but many physicians have used a so-called "Refund System" or "Token System," which makes the patient add 3s from his own pocket, so that the physician nets 10s, 6d per service. I shall not discuss the arrangements for specialist or laboratory services, but with this brief explanation will quote from Dr. Douglas Robb's book just published (*Health Reform in New Zealand*. Whitcomb and Tombs, Limited, 1947): "Under these schemes, the doctors have become extraordinarily prosperous. It is comparatively easy to work up a good income almost anywhere except, perhaps, in rural districts where a lot of travelling is still necessary. Actual figures of doctors' incomes are not published, but some which are almost fantastic are commonly mentioned in parliament. The highest rewards are obtainable under a company arrangement, where the principal can pay handsome salaries to juniors and still reap rich rewards. The individual man can make a big income by dint of hard work and organization. . . . From the doctor's point of view perhaps it is a good thing that by ordinary work he can secure very adequate rewards. . . . The emphasis is placed on the number of acts done rather than on quality. Indeed, we find the doctor personally doing a number of trifling things in his practice that ought to be done by a nurse or secretary, but are not so done because it is worth 7s 6d a time to the doctor, if he does them. . . . The poor man's cough is now as profitable as the rich man's, and certain areas both urban and rural formerly poorly served now have medical men on the spot. So far so good, but a further effect is to concentrate medical men in the cities as against country districts where travelling is greater. . . . Moreover, as between general practice and specialists, scientific and teaching work, there is a disproportionate attraction to the former. The pathologists, radiologists, hygienists, and teachers in the profession are almost

all maintained by salary and are the Cinderellas in the financial sense. . . . The quality of service suffers under the fee-per-service structure with its emphasis on quantity rather than quality. The tendency is toward quick superficial work and the avoidance of difficult subjects, times, and places."

According to the New Zealand system, the patient pays nothing for pharmaceutical benefits, but merely hands in his prescription and countersigns it when he receives his bottle. The total cost of pharmaceutical benefits has risen steadily and now reaches almost fantastic proportions. For the fiscal year 1945-1946, the cost to the government for payment to physicians was 1,633,514 pounds and the cost to the government for pharmaceutical benefits was 1,133,366 pounds, a figure only one-third less. The enormous proportions of the expenditure for pharmaceutical benefits reveals what must have happened, namely, the doctor reverted to the old method of satisfying the patient in the quickest way by giving a prescription. I believe it will be difficult now for New Zealand to extricate herself from the poor system on which the general practitioners have grown fat.

The New Zealand experiment teaches lessons. First, the medical care program was thrust on the country by the Labor Government without adequate consultation with medical groups. A chief reason for this was that organized medicine there was not conciliatory to change in medical care, like the British Medical Association in the Lloyd George regime and organized medicine in this country now. Thus, the medical care program was poorly thought out and designed. Second, it was commenced before the organization for medical care the country over was able to cope with it; it sought solution by removal of economic barriers alone. Third, the rank and file of general practitioners profited, as is bound to be the case in any medical care system in which the medically indigent become medically solvent, as they will do in this country as soon as the medically indigent group ceases to exist as such. It is astonishing that practicing physicians in this country do not see that their incomes will be increased the moment the medically indigent group becomes a secure source of revenue. But before leaving the account of the New Zealand experience with the fee-for-service method of reimbursement, I ought to caution against the impression that the medical care program there has been a failure. Whatever its defect in administration, it has made general practitioner service available to all and must have given feelings of security difficult to evaluate to low income groups particularly by removing the specter of pauperizing illness. The total success or failure of a medical care program can be measured in just one way, its results on the happiness and health of the people.

It is obvious that a *sliding fee-for-service* method of payment—I refer to our present system in which the physician has the right to charge what he thinks he can get—would vitiate, and hence be unworkable in any prepayment scheme which undertakes to furnish complete coverage medical care. But a regulated fee-for-service system has been used in Sweden successfully. However, I personally doubt if even the *regulated fee-for-service* method can be used successfully in any large prepayment program *including all medical services* in the complex conditions of this country, because it is so easily abused and difficult to control.

I shall not discuss other systems of payment to physicians in nationwide health plans except to say that in New Zealand and in England, physicians on the capitation method of payment have liked it, and capitation has many advantages, particularly in promoting preventive medical care. It is planned to try it in Baltimore for the care of the indigent as part of a plan, already endorsed by the Baltimore Medical Society, which is highly original and has great potentiality. Probably in any nationwide medical care system all three methods of remuneration, controlled fee-for-service, capitation, and salary have their places.

Now comes a subject which seems to me to be of great importance, namely, the participation of the medical schools in medical care plans, but there is time only to touch on it here and there.

First, there must be more physicians to cope with the increased burden of medical care under any plan which includes full care of all the people. Dr. Parran has supplied some figures in this regard. The medical schools of the country now turn out about 5,200 graduates a year. Adding the 7,000 graduates accrued as the result of accelerated war education, there would be produced, in the next twenty years (by 1957), 111,000 physicians. During the same twenty-year period, 77,000 would be lost from death or retirement. This gives an estimated net gain, by 1967, of 34,000 physicians. But the gain in population by 1967 will require 27,000 additional physicians to maintain the existing ratio of physicians to population. This reduces the net gain in 1967 of 34,000 physicians to 7,000. But a whole variety of unrelated factors, such as specialization and the increased complexity of medicine, the spread of prepayment plans of medical care, the inclusion of the medically indigent, the supply of the newly created health centers and hospitals, all unite to increase the requirement for physicians above the present physician-population ratio. To meet this, Dr. Parran calculates that by 1967 our medical schools must produce nearly 50 per cent more graduates than at the present time, 7,800 instead of 5,200. It follows that either the capacity of our medical schools must be increased or else new ones must be created. There would be great opposition at the Johns Hopkins Medical School to any large increase in the number of medical students because of a lack of expandable teaching facilities, and this attitude probably prevails in the other full-time medical schools. I personally hope very much that the increased demand for physicians will be met by the formation of new full-time medical schools which could then be placed in the areas of need just like the new hospitals and medical centers to be constructed under the Hill-Burton Act. But, though new hospitals and centers can spring up in two years, from seven to ten years at the least would be required to furnish the 50 per cent additional quota of physicians, and this means that to attain Dr. Parran's 50 per cent increase in the number of physicians by 1967, it will be necessary for the medical schools to plan on turning out 100 per cent more graduates immediately, that is, to double their admissions at once.

Second, our medical students should be better selected. The health of our people is so important that physicians should be as fine and intelligent a class as we possess. The standards in medical education ought to be high and the inducements to a medical career made great.

Third, medical education should be extensively reorganized and improved in two parallel ways. First, it should be integrated much more closely with public health, and the student should be taught to regard the prevention of disease to be as much his duty as the care of the sick. In the list of objectives which the Canadian Medical Association adopted for presentation to the Canadian Government, the first on the list is "The Promotion of Health and the Prevention of Disease." Preventive medicine, or the proper attitude toward it, cannot be taught by placing separate departments of preventive medicine in medical schools. Why not establish separate departments of therapeutics? Preventive medicine is an every-day, every-hour, every-minute part of clinical medicine, and must be taught by clinical teachers themselves in connection with their cases and daily work, and the teachers of clinical medicine must learn to reorient themselves and their duties to this philosophy. Then the teaching must be reorganized so as to give to the student a broad social viewpoint, so that he can join in a concerted effort to furnish medical help in all aspects to all people, with intelligence and enthusiasm. Finally, practical training in hospitals or centers should be at least three years, making the total period of preparation seven years before risking a young doctor on the community.

Fourth, the private medical schools must have state aid. At Johns Hopkins the tuition is $600.00 a year. The cost to the medical school of the education of the student is $3,900 per year. With the shrinking resources and the disappearance of the old private supports and without the addition of new, the full-time medical schools cannot continue.

Fifth, the State must aid the student financially because of the long, costly preliminary years of preparation, if medicine is to attract the finest of our young men. During four years in Johns Hopkins Medical School, the cost of the expenses of the medical student, apart from tuition, is from $1,300 to $1,500 a year. During his hospital training as intern, he receives no stipend. Only to those who command financial resources and can wait the years of preparation is a medical career open. If the State salaried the young doctor during his three that was over it would be fair for the State to draft him on a salary basis for two years of hospital experience, a great part of the load would be lifted and after to three years for some rural community where physicians were required. This idea is suggested in the proposals of the Canadian Medical Association to the Canadian Government. A somewhat similar plan has been introduced into the medical care scheme of North Carolina. The plan would be similar to that now in operation in our naval and military academies.

Sixth, I now come to an idea of the greatest importance, namely, that the medical schools must agree to extend their teaching obligations to the practicing physicians. One of the worst features in our present system of medical care is that practicing physicians of the community have no adequate means of keeping up with medical progress and, in consequence, are left in intellectual, quickly turning to spiritual, stagnation. Of course, many, of the more progressive practicing physicians go to medical schools for refresher courses yearly or attend medical meetings where practical surveys of various topics in medicine are given by experts. But the education of practicing physicians ought to be organized so

as to be a regular part of their professional lives. Of course, medical schools could offer refresher courses, but by general admission this method is not the best way to teach. The method which has tremendous possibilities is for the medical schools to extend their activities into the subsidiary or satellite hospitals and centers created by the Hill-Burton Act. I do not know quite how the plan could be best worked out, but suggest that the Medical Schools send to the satellites on some rotation plan, groups of their able, splendidly trained specialists in internal medicine, pediatrics, surgery, x-ray, pathology, biological chemistry, etc., with the understanding that these men act as heads of the general services in their respective fields, consultants, and teachers. These emissary representatives of the medical school faculties would be full-time workers on salaries and would not compete with local physicians. The salaries would have to be good ones, and furnished to the medical schools by the State, for the medical schools must be given complete freedom. I also suggest that medical schools supply the satellite hospitals and centers with interns, who would work under their emissary preceptors from the medical school just as at the home hospitals. By general agreement, the finest medical care anywhere in this country is that furnished by the medical school hospitals, and the suggestion made would give the remote communities that same splendid level of care. The teachers assigned to the satellites could give clinics and systematic instruction of various kinds to the practicing physicians, and, much more important, could go over their patient problems with them in the home, out-patient clinic, ward, operating room, or laboratory. There is no teaching so good for teacher or student as case teaching. This extension of the medical schools to include the education of the practicing physicians would have the greatest influence I can conceive of in raising the morale, the standards of work and the enlightenment of the medical profession of the nation. I make one further suggestion, that if the private medical schools will not or cannot enter into this plan, the State subsidize the State-supported medical schools and create, where needed, new full-time State schools of medicine whose particular duty it will be to organize and furnish instruction to the practicing physicians, which will keep them abreast of medical progress.

A participation of the medical schools in medical care is envisioned in the National Health Service Bill for England and Wales.

As intimated, the policy of gradual development of a medical care program has its perils, and the perils are that the moves forward will be in wrong directions or will lead into pits, like the thinly concealed ones in the Taft Bill, or remain isolated when they ought to be coordinated. Gradual development is the best policy, provided it is carefully thought out, but it is dangerous if not thought out at all. Take the Hill-Burton Act for example. This was designed to make available the latest advantages of group medicine to the needed areas. Where will the specialists who are to form the groups come from? They will not spring from a ground sown with dragon's teeth like the robot warriors in the fairy tale. They cannot be enticed to rural areas by the prospects of large fees. If the attraction must be good salaries, then a little planning could bring the wonderful, uplifting influence of the medical schools into the program. Again, the construction of the hospitals and the centers makes at once an increased

demand for physicians; yet, as pointed out, physicians, and specialists in particular, are seven-year products at least, and yet no steps have even been contemplated to increase the output of the medical schools. Granted that it is impossible now to think through the problem of medical care to the very end, it is certainly possible to think a considerable way into it; some requirements are common to any comprehensive medical care plan, and are as evident now as twenty years away. There is no planning in what is going on, and this is because there is no medical leadership. The movements such as voluntary insurance and the isolated experiments in medical care were born in the minds of enterprising, socially conscious groups of physicians or lay organizations working outside organized medicine. If organized medicine had been responsible for these isolated attempts, even if unable to formulate any complete program of its own, it would have much to its credit. It, nevertheless, should have furnished the leadership, but not only has it not shown leadership, but has opposed important developments which have gone on. In spite of its dead weight, and resisting on occasions, organized medicine has been dragged forward by the sheer power of outside opinion and the force of example elsewhere, a long way since 1938, when it tried to block the formation of the Washington Group Health Association, until now it endorses the nonprofit prepayment or voluntary insurance principle, and recognizes the necessity under certain conditions of Federal Aid in medical care plans. But its much touted "Ten-point program" is no program in any original, dynamic, or constructive sense, or, indeed in any sense, but only a series of pious platitudes or highly qualified endorsements of policies or activities, initiated in the first instance by isolated groups of liberal minded, socially conscious physicians or laymen working independently of it. Its primary concern throughout as judged by its behavior has seemed to me to be aimed consistently at the preservation of the medical care system as it exists today at all costs. Disturbed, it cries out in the words of Fafnir coiled around his treasure, when the youthful Siegfried, the personification of the new order, approaches with his magic sword, "Lass mich schlaffen."

In this critical period of change, when the handwriting appears on so many walls, the behavior of organized medicine is humiliating, and its leadership has seemed incredibly stupid in contrast to the up-and-coming, progressive attitude of the Canadian Medical Association, which has boldly and unqualifiedly taken the leadership and presented to the Canadian government their own plan for a system designed to provide comprehensive medical care for everyone. When I asked a prominent Canadian physician how it happened that the Canadian Medical Association was so open- and liberal-minded, he replied, "We saw what was coming and decided it would be better to develop our own program, one which we liked, rather than to have one forced on us. He remarked further, "We have some big leaders." I think that Dr. Fishbein has had an opportunity, such as comes to few, to lead organized medicine in our country in a program of medical care which would have been a monument to an enlightened and progressive spirit, but he chose the opposite course, the course popular and easy at the moment but not the one destined to appear creditable in history. Without leadership, it is impossible to concert a plan, but I express the view that fresh

legislation should be introduced into Congress along a middle ground between the proposals of the Wagner-Murray-Dingell Bill on the one side and the Taft Bill on the other, legislation which, among other things, would give the Federal government enough authority to develop and maintain the general structure and standards of a comprehensive medical care system, but would allow the individual states freedom to develop their own programs within the general outline; which would preserve private practice, as it now exists, for the upper income groups, but would make medical care available through a *government* insurance scheme to the lower income groups, not merely general practitioner service but the most intelligent broad-reaching medical care which scientific progress and specialization through group practice have now made possible anywhere and which, finally, would augment and implement existing medical schools and establish new ones in needed areas, so that they could turn out annually the requisite number of excellent physicians and could assume regionally the continuous education of the practicing physicians as a regular part of their duties, preferably through extension into the newly created hospitals and centers.

A few weeks ago President Truman requested the Federal Bureau of Investigation to investigate all government employees in order to discover and eliminate Communists. I sometimes think that governments are more in need of psychiatrists than are individuals. The way to free this country from Communism is not by Gestapo espionage and persecution, methods which history has shown over and over and over again merely drive ideologies underground and give them increased impetus by repression and dispersion, but to make our own people so much better fed, housed, clothed, and educated and happier and freer than others, that Communism will wither and die for lack of soil of misery and discontent to grow on. I can think of no better beginning than with the least possible delay to reorganize medical care so that in full measure and in most modern kind it would be available to each citizen with all its benefits.

THE ADEQUACY OF ARTIFICIAL FEEDING IN INFANCY

STUART SHELTON STEVENSON, M.D.*
BOSTON, MASS.

If health and strength permit thee, don't refuse
The child thy nipple; nor another's use—
Yet if thou'rt sickly, if thy spirits fail,
If the child's touch'd with any catching ail,
This duty, whether hated or desir'd,
Ceases, and 'tis no more of thee requir'd.
Then not to suckle, is not to neglect,
But chuse a nurse, and I'll thy choice direct.

Scevola de Sainte-Marthé (1526-1623)[1]

THE natural and preferred way to feed the human infant is at his mother's breast if this is feasible and practical. After a period of relative neglect of the breast feeding of babies, the pendulum has now swung so far in occasional clinics that the more ardent advocates of human milk would seem to have lost some objectivity in their arguments. Scevola's advice, which is quoted above, may be worth heeding: today we do not have wet-nurses available in practical supply, but it is obvious that many thousands of infants are being reared successfully on cow's milk mixtures. It seems pertinent to review the objections to cow's milk as an infant food and to look impassionately into the facts concerning the adequacy of artificial feeding in infancy.

OBJECTIONS TO COW'S MILK AS AN INFANT FOOD

A. The Protein in Cow's Milk Is Inadequate: It Consists Mostly of Casein and Casein Is Low in Cystine, an Essential Amino acid.—The large amount of total protein in cow's milk and the appreciable amount of lactalbumin which it contains help to make up for the deficiency of cystine. Recent work[2] suggests that casein is utilized as well as lactalbumin by human beings.

For many years, Powers (unpublished data) has fed premature infants successfully on cow's milk mixtures and growth has been satisfactory. Gordon and his associates[3] have confirmed this and shown, further, that premature infants who are fed upon cow's milk mixtures gain weight faster than when they are fed isocaloric amounts of human milk.

Infants who are fed upon cow's milk continue to increase the percentage of the nitrogen content of their bodies at a rate approximating the fetal increase. If they are fed upon human milk, containing less than half as much protein, the percentage of the nitrogen content of their bodies remains at the birth level or decreases slightly over a period of many weeks.[4] It would seem that the protein of cow's milk is adequate.

From the Department of Maternal and Child Health, Harvard School of Public Health.
*Assistant Professor of Child Health, Harvard University.

B. The Fat of Human Milk Is More Suitable for Human Ingestion.—This is apparently not true.[5] Furthermore, Gordon[3] has shown that premature infants gain more rapidly when the percentage of calories offered as fat is halved, presumably because of the inability of small infants to utilize any kind of fat adequately.

C. The Calcium of Human Milk Is Better Utilized by the Infant Because of a More Favorable Calcium-Phosphorus Ratio.—This is probably true. But cow's milk contains four times as much calcium as human milk and the percentage content of calcium in the infant's body increases steadily, after a small drop in the first few weeks, if he is fed cow's milk. By the end of his first year, he has a much higher relative calcium content than he had at birth. On the other hand, the infant fed human milk sustains a relative calcium content loss for many weeks and at the end of the first year of life the relative calcium content of his body is below what it was at birth.[4] There is no evident harm in the extra calcium storage which the infant achieves when he is fed cow's milk.

D. Cow's Milk Is Not Well Digested by the Infant.—It is now recognized that this indigestibility results from the large curds which casein forms when acted upon by rennin in the infant's stomach.[6] Present-day feeding mixtures offer denatured casein which forms soft, small, digestible curds.

E. Artificial Feeding Mixtures Are Difficult for the Mother to Make.—It would seem that this objection arose out of the complexities of the formulas of thirty years ago. The modern feeding mixture of milk, sugar, and water requires little mental dexterity for its preparation.

F. Artificial Feeding Is More Expensive.—This may be true when calculated only in terms of the money spent for the ingredients. When it is realized that the average woman ingests an inadequate diet and shows no present disposition to change her eating habits, then it must be admitted that lactation presents a serious drain on the mother which may be of incalculable expense to her future well-being. Furthermore, the modern mother must not infrequently work at a part-time job to complement the family income. Obviously she cannot work and be at home to nurse her infant.

G. Artificial Feeding Does Not Satisfy the Infant's Psychic Needs.—The infant evidently gains needed satisfaction from the exercise of his sucking reflex during feeding. A sufficiently small opening in the rubber nipple would seem to offer him pleasure as great as he would obtain from sucking at the breast.

It seems desirable that the infant should be fondled and loved during his feeding if he is to be properly conditioned toward food and perhaps toward life in general. This fondling, offered automatically by the mechanics of breast feeding, can be supplied to the artificially-fed infant if the mother is properly instructed.

If the infant gains such psychic satisfaction at the breast as we have been led by some to believe, it seems surprising that almost every infant, if he is being fed by both methods, prefers the bottle. Psychic satisfaction will not be achieved for the infant unless the milk supply is adequate. Artificial feeding offers the easier means of ascertaining this adequacy and gives the mother peace

of mind when she satisfies her human desire to know how much milk her baby has ingested. Parenthetically, it might be noted that many modern women do not seem to satisfy any maternal urge by suckling their young.

H. Artificially-fed Infants as a Group Suffer from a Higher Morbidity and Mortality Rate.—We have already stated that we consider breast feeding the natural and preferred way to feed a human infant. Obviously the most unintelligent mother can usually manage to offer her breast to her infant without mishap. But the errors of an unintelligent mother should not militate against the artificial feeding of an infant by a capable mother when this seems the necessary or more practical method.

It is true that artificially-fed infants suffer from a higher morbidity and mortality rate. This would seem to constitute the most important, valid objection to the artificial feeding of infants, and it is worth while to review this matter in some detail.

MORBIDITY AND MORTALITY IN THE ARTIFICIALLY-FED INFANT

A. In the Papers of Grulee and His Associates[7, 8] *Which Have Become Classic Arguments for Breast Feeding, Certain Facts Are Apparent.*—

1. Twenty thousand Chicago infants were studied between 1924 and 1929. That they received good medical and nursing supervision in infant welfare conferences becomes evident in the fact that their over-all mortality was four times as low as the infant mortality then prevailing in Chicago. The series was adequate in numbers and the artificial feeding was presumably carried out in a better than average manner.

2. Breast-fed infants showed a mortality of only 1.54 per thousand while artificially-fed infants suffered a mortality of 84.36 per thousand. This is a ratio of 1 to 56.

3. Ten per cent of all the deaths were attributed to gastrointestinal disturbances, 30 per cent to miscellaneous causes and 60 per cent to respiratory infections. It is reasonable to assume that a certain percentage of the gastrointestinal deaths were the result of parenteral diarrhea caused by respiratory infection. The respiratory mortality ratio of the breast-fed infants to that of the artificially-fed babies was 1 to 115, whereas similar ratios for gastrointestinal disease and miscellaneous causes were only 1 to 40 and 1 to 27 respectively. Thus the majority of the deaths among artificially-fed infants was due to respiratory infections.

4. The mortality rate from respiratory infections did not differ greatly in the breast- and artificially-fed infants until after the fifth month of life. Then the mortality from this cause in the artificially-fed group soared and accounted for much of the increased mortality of this group.

5. This work was done in the years 1924-1929. While the feeding mixture used was essentially comparable to those employed today, the vitamin complementation of the diet was inadequate by current concepts. Thus, the infants began to receive orange juice at 4 weeks of age: a daily amount of ½ teaspoon was increased slowly to 8 teaspoons by the age of 5 months. They began to

receive cod liver oil at 6 weeks of age: a daily dosage of 10 drops was increased gradually to 3 teaspoons by the age of 5 months.

B. From the Work of Ebbs and Mulligan,[9] Further Facts May Be Summarized.—

1. One thousand five hundred infants under one year of age admitted to the hospital with infections were studied.

2. Of these infected babies, 15.1 per cent had been breast fed, whereas 35.6 per cent of the babies in the city's well-baby clinics were being breast-fed. In other words, the incidence of breast feeding among the infants admitted for infection was less than half the incidence in the city well-baby clinics.

3. Respiratory infections accounted for 73.7 per cent of the hospital admissions, and gastrointestinal infections accounted for another 20.9 per cent. Thus respiratory infections accounted for a majority of the illnesses.

4. The mortality of breast- and artificially-fed infants was essentially the same: 18.5 per cent for the breast-fed infants and 16.4 per cent for the artificially-fed babies.

C. The Records for the First Year of Life of 263 Infants Have Been Analyzed by the Writer.—These infants were carefully followed in connection with a longitudinal study of child health and development which is still in progress in the Department of Maternal and Child Health of the Harvard School of Public Health. The methods adopted in this comprehensive study have been described in a former publication from this department.[10] The records being considered here were obtained during the years 1930 to 1940. Certain facts seem pertinent:

1. Ninety-five infants were breast fed for three months or longer; 113 infants were partially breast fed; fifty-five infants were entirely artificially fed. The series is selected, in that only those records which were complete for the first year of life were analyzed. This implies that these infants had mothers with the initiative and desire to cooperate which regular attendance at the study clinic required. The economic and social strata of the infants were varied. Growth and development of the entire group were, in general, satisfactory.

2. The cow's milk feeding mixtures which were used supplied about 55 calories per pound of infant body weight. One-third to one-fifth of the total calories was in the form of added carbohydrate.

3. Orange juice and plain cod liver oil were begun on all the infants before the second week of life and the amounts increased as rapidly as tolerated until 4 ounces of orange juice and 2 teaspoons of cod liver oil were being given daily. Thus it was planned that each baby would be receiving a daily complement of approximately 60 mg. of ascorbic acid, 6,300 I. U. of vitamin A, and 630 I. U. of vitamin D by the time he was a few weeks old.

4. The illnesses of each infant were tabulated as respiratory, gastrointestinal, and other infections. The respiratory infections were further tabulated as upper respiratory infections, without fever, of at least two days' duration; and as respiratory infections with fever. The latter category includes the complications of such infections as otitis media cervical adenitis, and pneumonia.

The gastrointestinal infections, for the most part, were diarrheas with no obvious parenteral cause; many of them may have been gastrointestinal upsets without infection as a basis. The great majority of the other infections were of the skin, such as impetigo and furuncles.

5. The dietary intake during pregnancy of ascorbic acid and vitamin A of the mothers of these infants was carefully ascertained as described in detail in the publication referred to previously.[10] There is no correlation between either the amount of ascorbic acid or Vitamin A taken prenatally by the mother and the number of infections in her infant. This is not an unexpected finding with respect to ascorbic acid when it is recalled[11-13] that the cord blood of the newborn infant is two to four times richer in ascorbic acid than the mother's blood at the same time. The differential is greater when the maternal plasma level of ascorbic acid is lower and the fetus seems to act as a parasite to a degree upon its mother with respect to this vitamin. The mother's prenatal intake of vitamin A would not be expected to affect the infant, within limits, when it is recalled[14, 15] that gross saturation of the mother with vitamin A (up to 400 I. U. per 100 c.c. of plasma) does not affect the level of vitamin A in the cord blood. Furthermore, Dann[16] has shown that the small amount of vitamin A in the liver of the newborn rat cannot be increased by feeding the mother rat large amounts of the vitamin during pregnancy.

6. Table I shows the percentages of breast- and totally artificially-fed infants in the series (150 infants tabulated here) who suffered with one or more infections of the three types, during the first year of life.

TABLE I. PERCENTAGES OF BREAST- AND ARTIFICIALLY-FED INFANTS SUFFFERING FROM ONE OR MORE OF THE DIFFERENT TYPES OF INFECTIONS

TYPE OF INFECTION	PERCENTAGES OF INFANTS INFECTED
Respiratory	85.3
Gastrointestinal	27.0
Other	21.4

It is evident from Table I that respiratory infections, affecting 85.3 per cent of the infants, are the major cause of illness in all infants under one year of age regardless of the method of feeding.

7. Table II shows the average number of infections per infant, of each type, tabulated according to the method of feeding.

The increased amount of diarrhea in the partially breast-fed group would seem to have resulted from the fact that these infants as a group represented the more difficult babies and/or mothers. When their records are studied, it becomes evident that attempts were made to have the mothers continue breast feeding at a time when there did not seem to be sufficient milk or the infant

TABLE II. AVERAGE NUMBER OF INFECTIONS PER INFANT ACCORDING TO METHOD OF FEEDING

TYPE OF INFECTION	BREAST-FED	PARTIALLY BREAST-FED	ARTIFICIALLY-FED
Respiratory	1.56	1.71	2.18
Gastrointestinal	0.10	0.23	0.12
Other	0.13	0.13	0.13

was not thriving on breast milk or the mother thought he was not. Not infrequently these mothers complemented their breast milk with self-concocted feeding mixtures. It does not seem profitable to attempt further analysis of this partially breast-fed group.

There is a statistically significant difference between the average number of respiratory infections in the breast- (1.56) and the artificially-fed (2.18) infant. There is no significant difference between the two groups with respect to gastrointestinal and other infections. It is evident from Table II that respiratory infections constitute a special problem of the artificially-fed infant.

8. Table III shows the percentages of infants who suffered from respiratory infections. These are tabulated according to the method of feeding and the series is broken down to show percentages of upper respiratory infections of two days' or more duration without fever, and of respiratory infections with fever.

TABLE III. PERCENTAGES OF INFANTS SUFFERING FROM ONE OR MORE RESPIRATORY INFECTIONS

TYPE OF INFECTION	PERCENTAGE OF INFANTS INFECTED	
	BREAST-FED	ARTIFICIALLY-FED
Respiratory (all types)	80.0	94.5
URI without fever	56.9	60.0
Respiratory with fever	23.1	34.5

There is a statistically significant difference between the percentages of breast- (80 per cent) and artificially-fed (94.5 per cent) infants suffering from one or more respiratory infections of all types. The percentages of infants of both feeding categories who contracted one or more upper respiratory infections without fever (56.9 per cent and 60.0 per cent) are proximate. This suggests that the amount of exposure to respiratory infections was not greatly different in the two groups. The percentages of the two categories of infants who had one or more respiratory infection with fever (23.1 per cent and 34.5 per cent) are not significantly different, but there is a numerical advantage to the breast-fed infant. This suggests that the artificially-fed infant, with exposure equivalent to the breast-fed baby, does not have the same resistance as the latter and allows his upper respiratory infection to develop into a more serious disease. Furthermore, it is evident from Table II that the artificially-fed infant suffers from more repeated respiratory infections than his breast-fed colleague.

9. Table IV shows the average number of respiratory infections of all kinds per infant for each quarter of the first year of life. They are tabulated according to the method of feeding.

There is no significant difference between the number of respiratory infections per infant (0.61 for breast-fed; 0.75 for artificially-fed) in the two feeding

TABLE IV. AVERAGE NUMBER OF RESPIRATORY INFECTIONS PER INFANT PER THREE-MONTH PERIOD

METHOD OF FEEDING	NUMBER OF RESPIRATORY INFECTIONS PER INFANT			
	0-3 MO.	3-6 MO.	6-9 MO.	9-12 MO.
Breast	0.24	0.37	0.36	0.59
Artificial	0.29	0.46	0.65	0.78

categories during the first six months of life. However, there is a statistically significant difference in the numbers for the second six months of life (0.95 for breast-fed, 1.43 for artificially-fed). This is reminiscent of Grulee's findings.[8] It is evident from Table IV that the artificially-fed infant in his second half year of life does not have the resistance to respiratory infection which the breast-fed infant enjoys, even though the breast-fed infant may have been weaned at the age of 3 or 4 months.

D. Comparison of Data.—In the comparison of morbidity and mortality rates in breast- and artificially-fed infants it is well to remember that breast-fed infants probably represent a series which tends to be selected for its more solicitous mothers. Grulee's study and the one which is reported here would seem to minimize this complicating factor.

The data from three clinics which are presented above are not strictly comparable: Those of Grulee concern only mortality;; those of Ebbs concern only hospitalized infants with varied fates; data presented here are from a much smaller series. However, certain facts may be summarized:

1. The great majority of illnesses in infancy are respiratory, regardless of the method of feeding.

2. The increased incidence of respiratory infection in the artificially-fed infant occurs during the second half year of life.

3. The artificially-fed infants of Grulee's series, with their greatly increased mortality, were given vitamin complements which are inadequate when judged by current standards.

4. In the series of infants presented here who were given complements of vitamins currently considered to be adequate, there is no significant increase in the incidence of gastrointestinal and other infections in the artificially-fed group. The increase in respiratory infections in this group is relatively small and occurs during the second half year of life.

5. In the series of infants presented here, there is an increase in the incidence of diarrhea among the partially breast-fed infants which may be related to attempts at forcing an unwilling mother into continued breast feeding.

6. There is no correlation between the mother's intake of ascorbic acid and vitamin A during pregnancy and the amount of infection in her infant.

7. Valid objection to the artificial feeding of infants would seem to be based upon an increased amount of respiratory infection in the second half year of life.

THE MODIFICATION OF PRESENT-DAY ARTIFICIAL FEEDING

It has been shown that artificially-fed infants do not suffer from more diarrhea than do nurslings when the feeding is carried out with proper technique. But it has not been possible to effect a decrease in the incidence of respiratory infections in these babies which would seem commensurate with the increased precautions against infection. Data have suggested (Table III) that exposure to respiratory infection is not greatly different in the breast- and artificially-fed infant. This implies that host resistance, rather than exposure to the infective agent, as in the case of many diarrheas, is the factor which

determines clinical respiratory infection in the infant. It is worth noting that Sargent and his associates[17] have recently suggested that a constitutional factor is important in the etiology of the common cold in adults.

What is the basis for this greater resistance to respiratory infections which the breast-fed infant seems to possess during his second one-half year of life? Protection by the known passive antibodies which are transferred through the placenta lasts usually only through the first one-half year of life. Most infants are not breast-fed beyond 6 months of age, yet the increased respiratory resistance of the breast-fed infant becomes evident after the infant is weaned, and remains effective for many months. Long duration of protection is not a recognized virtue of passive antibodies of any variety. The mother's immunity to respiratory infections is short-lived and inadequate at best. It does not seem probable that such immunity could be supplied to the breast-fed infant in the form of passive antibodies either transplacentally or in the breast milk. Rather it seems likely that some substance or substances contained in breast milk are stored in the body of the breast-fed infant which are important to his resistance to respiratory infections long after breast feeding has been discontinued. A comparison of human and bovine milks may suggest what these substances are.

A. Comparison of Human and Bovine Milk.—Human and bovine milks show certain differences in composition. Their protein and calcium contents have been discussed above. It is accepted that the importance of their approximately equal deficiency of iron is minimized by the fact that the infant is born with a store of iron usually sufficient to the period of his milk diet.

Their differences in vitamin content are tabulated in Table V, which is modified from the paper of Lawrence and associates.[18]

TABLE V. VITAMIN CONTENT OF HUMAN AND COW'S MILK

VITAMIN CONTENT	HUMAN MILK (PER 100 C.C.)	COW'S MILK (PER 100 C.C.)
Thiamine (μg)	14	38
Riboflavin (μg)	37	200
Nicotinic acid (μg)	183	85
Vitamin D, U. S. P. units	0.4 to 10	0.5 to 4.0
Ascorbic acid, mg.	5	2
Vitamin A (μg)	65	33
Carotene (μg)	25	30

Raw cow's milk contains more than twice as much thiamine as does human milk (38 vs. 14 μg per 100 c.c.), and the usual loss of thiamine in the processing of cow's milk varies from a usual 10 per cent to a maximum 60 per cent.[18] This means that even boiled cow's milk remains a richer source of thiamine. Raw cow's milk contains about five times as much riboflavin as does human milk (200 vs. 37 μg per 100 c.c.) and the loss of this vitamin in processing is not excessive.[18] Human milk contains about twice as much nicotinic acid as does bovine milk (183 vs. 85 μg per 100 c.c.) but its significance for the infant is not clear. Both milks contain inadequate amounts of vitamin D and it is generally believed that all infants should receive additional vitamin D in their dietary.

It seems noteworthy that human milk contains two and one-half times as much ascorbic acid as does raw cow's milk (5 vs. 2 mg. per 100 c.c.), and boiled cow's milk contains almost none. Even the daily 30 mg. of ascorbic acid which is recommended for the 6-month-old infant[19] does not approach in quantity the 48 mg. contained in a quart of human milk. It is further noteworthy that human milk contains about twice as much vitamin A as does cow's milk (65 vs. 33 μg per 100 c.c.), and an approximately equal amount of carotene (25 vs. 30 μg per 100 c.c.). One quart of cow's milk thus contains the equivalent of approximately 1,700 I. U. of vitamin A (if 0.25 μg of vitamin A and 0.6 μg of carotene are considered to be equivalent to one I. U. of vitamin A activity). Because this more than supplies the daily 1,500 I. U. recommended for the 6-month-old infant,[19] artificially-fed infants not infrequently receive no additional vitamin A in their dietary. But the breast-fed infant is receiving approximately 2 900 I. U. of this vitamin in each quart of human milk.

It is apparent that the breast-fed infant who ingests one quart of human milk, even without vitamin complementation to his dietary, receives considerably greater quantities of vitamin A and ascorbic acid than the artificially-fed infant who is fed by recommended standards and drinks a quart of cow's milk in the process. In practice, this differential is even greater when infants are fed isocaloric amounts of the two milks because carbohydrate is added to cow's milk in the usual artificial feeding mixture and the amount of these vitamins in 100 calories of mixture fed is less than in 100 calories of cow's milk. If one might argue teleologically, nature is not usually extravagant and the relative abundance of these two vitamins in human milk seems noteworthy.

It is also important that the breast-fed infant seems to utilize ingested ascorbic acid better than the artificially-fed infant. Snelling[20] reported that a group of thirty-one breast-fed infants, with an average daily ascorbic acid intake of 35 mg. obtained from breast milk, showed plasma ascorbic acid levels averaging 0.76 mg. per 100 c.c. This value could not be raised even when these breast-fed babies were given orange juice as a complement to their mother's milk. On the other hand, a group of seventy-nine artificially-fed infants, with an average daily ascorbic acid intake of 30 mg. obtained from two or more ounces of orange juice, showed plasma ascorbic acid levels averaging only 0.30 mg. per 100 c.c. Breast milk may enhance the absorption of this vitamin, or the ingestion of it in breast milk at frequent intervals throughout the day may allow of more complete absorption. Dann[21] has shown, furthermore, that infants ingesting boiled breast milk show significantly higher plasma ascorbic acid levels after receiving a complement of the vitamin than do infants ingesting boiled cow's milk who received an equal amount of the vitamin. She repeats the suggestion of Levine and his colleagues, [22] that the greater amount of protein in cow's milk increases the infant's need for ascorbic acid.

A report by Daniels[23] suggests that the breast-fed infant absorbs ingested vitamin A more completely than does the artificially-fed infant.

The breast-fed infant not only receives greater quantities of ascorbic acid and vitamin A than the artificially-fed infant, but he seems to absorb them more completely or, in the case of ascorbic acid, perhaps has less need of this vitamin.

B. The "Recommended Dietary Allowance" of Vitamin A in Infancy.—The recommended dietary allowance of vitamin A for the 6- to 8-month-old infant is 1,500 I. U.[19] Because there is not yet any generally accepted method for determining the daily requirement for vitamin A, because the amount required varies according to the percentages in the diet represented by vitamin A and carotene, and because body storage of the vitamin complicates balance studies: "Greater divergence of judgment exists as to the requirement for vitamin A than for any other dietary essential."[19] Most estimates of the human requirement are based on studies of the amount needed to maintain normal dark adaptation of the eye. Dark adaptation is, for practical purposes, impossible to study accurately in the infant. The National Research Council was forced to take the maximum estimated adult requirement which seems to be related to body weight and assume that the infant's requirements per pound of body weight were higher than the adult's. To allow for this assumed increased infant requirement, the calculated requirements were arbitrarily multiplied by the factors which represent the infant's increased protein requirement per pound of body weight. Thus the figure of 1,500 I. U. was obtained. It should be noted that no reference whatever is made, in the calculation of this figure, to the amount of vitamin A that the nursling obtains. This approximates 3,250 I. U. daily for an average 6-month-old breast-fed infant, if it be assumed a 15-pound infant ingests 47 calories per pound per day.

C. The Infant's Need for Vitamin A.—The infant's need for vitamin A was emphasized in Bloch's classic paper[24] in which he noted that xerophthalmia was a characteristic of vitamin A deficiency in growing animals; that it occurred early in infants on a vitamin A deficient diet and appeared in older children only after an absolute lack of the vitamin for a long period of time. He stated that he had never seen a case of xerophthalmia in a breast-fed infant. He emphasized that vitamin A deficient infants were frequent victims of respiratory infections and otitis media. In this connection, Boynton's[25] statement is pertinent: "Increased susceptibility to infection is apparently an early manifestation of a dietary low in vitamin A, having marked influence before the physical signs of deficiency are present."

The blood level of vitamin A is low in the newborn infant and drops still lower on the third day of life.[26] This third day drop still occurs when the infant is given a large amount of vitamin A during his first two days of life, and suggests either that the newborn organism is storing the vitamin at a rapid rate in its tissues or that utilization of the vitamin is great in the infant. Rapid storage seems a not unlikely explanation when it is recalled that the amount of vitamin A in the newborn liver is very small or nil,[27, 28] and that there is no evident limit to the infant's capacity to store vitamin A.[29]

Colostrum contains three times the amount of vitamin A and ten times the amount of carotenoids found in mature human milk.[30] It seems reasonable to imply that this fulfills an increased need of the newborn infant for the vitamin.

The blood vitamin A level of the infant continues to be low through his first six months of life and averages 75 I. U. per 100 c.c. It does not reach the average level of older children (110 to 117 I. U. per 100 c.c.) until after one year,

although it is possible to raise it almost to this level (93 I. U. per 100 c.c.) by 17,000 I. U. daily doses added to the diet.[31] These facts again suggest that the infant is either storing and/or utilizing vitamin A at a rapid rate.

May and his associates[32] showed that blood levels of vitamin A in infants, already low, decreased still further in the presence of fever and infection. They found there was a sharp drop in the blood level within a few days after placing an infant on an evaporated milk feeding mixture and suggested that "the amount of vitamin A customarily supplied to infants in ordinary whole cow's milk formulas may be scarcely sufficient to maintain an optimal level of vitamin A in the blood."

In 1923, Daniels[33] wrote: ". . . one is led to wonder whether the excessive reaction to infection which takes place in the artificially-fed baby is due to the fact that the protective substance (fat-soluble A) has been given in insufficient quantities or has not been absorbed from the alimentary tract in sufficient quantity."

It seems unnecessary to review here the extensive literature which deals with the relation of vitamin A deficiency to decreased resistance to respiratory infections. Attempts have been made to prove that the administration of vitamin A is without effect in increasing the infant's resistance to these infections but in many cases the infants studied were less than 6 months old, an age before the number of respiratory infections begins to increase, or they were receiving sufficient vitamin A in their basal diet to prevent deficiency. It seems probable that the newborn infant, with little reserve of vitamin A and an evident need for it, may suffer from a deficiency of it relatively quickly when the amount in his diet is inadequate and his absorption of it is poor. The artificially-fed infant receives less vitamin A than does the breast-fed infant and the probability of his suffering from a vitamin A deficiency cannot be overlooked.

The evidence suggests that vitamin A may be one of the substances contained in human milk which is stored in the breast-fed infant's body and enhances his resistance to respiratory infections. There is no reliable method for estimating the daily need of the artificially-fed infant for this vitamin, but it would seem reasonable to allow him a daily intake at least as large as he would obtain from breast milk. This would approximate 3,250 I. U. for a 6-month-old infant or 220 I. U. per pound of body weight and, as Clausen states,[34] ". . . if vitamin A has any anti-infective power, it should be administered in the earliest months when the growing organism may need large quantities, and when a deficiency is more likely to exist." There is no obvious reason why this administration should not be begun during the first week of life.

D. The "Recommended Dietary Allowance" of Ascorbic Acid in Infancy.—The recommended dietary allowance of ascorbic acid for the 6 to 8-month-old infant is 30 mg.[19] This figure was derived from various studies which show the lowest level of intake of the vitamin which will maintain "adequate" stores as judged by both the blood level of ascorbic acid and urinary excretion tests. The value thus derived represents "amounts well above the minimum needed to protect against scurvy, but below those needed for saturation." As in the

case of vitamin A, no reference is made to breast milk in calculating this recommendation of 30 mg., although the average breast-fed infant of 6 months, if it be assumed a 15-pound infant ingests 47 calories per pound per day, receives 54 mg. daily. And no definition of "adequate" stores is attempted.

Ascorbic acid presumably is stored in the infant's body, for it is common knowledge that it takes an infant several months to develop scurvy on a scorbutic diet and it seems no more reasonable to judge the amount of ascorbic acid in the infant's body by the blood level of the substance than it would be to judge the amount of glycogen in the body by the level of the blood sugar. It is not feasible here to review the literature which deals with the many functions of ascorbic acid in the body, but the prevention of scurvy in the infant would not seem to be sufficient proof of the adequacy of his ascorbic acid intake.

E. The Infant's Need for Ascorbic Acid.—The infant's need for ascorbic acid even at the time of birth becomes evident from the fact that his cord blood contains two to four times as much of the vitamin as his mother's blood at the time of delivery, [11-13] and that the blood of the umbilical vein contains twice as much ascorbic acid as the blood of the umbilical artery.[35]

Unlike fat-soluble vitamin A, ascorbic acid is evidently transferred across the placenta with ease. But the infant's need for ascorbic acid must be great or his storage of it poor for Mindlin[12] found plasma levels of the vitamin averaging 1.16 mg. per 100 c.c. within twenty-four hours after birth, 0.74 mg. per 100 c.c. at forty-eight hours, and 0.67 mg. per 100 c.c. at 72 hours of age. He suggests that the rapid formation of mesodermal tissues in the infant creates a great need for ascorbic acid with its important function in the formation of mesodermal intercellular substance.

Evidence has been quoted above[20, 21] which shows that ascorbic acid is better absorbed or less needed when it is ingested with breast milk. Mindlin[36] studied a group of 2-week-old infants and found an average plasma level of 1.0 mg. per 100 c.c. in the breast-fed group while the plasma level of the artificially-fed group averaged only 0.4 to 0.7 mg. per 100 c.c. even with 20 to 75 mg. of ascorbic acid added to their daily diet. The levels in the group fed artificially were obtained sixteen hours after oral administration of the vitamin, and it is suggested that ingestion of ascorbic acid at more frequent intervals, as with breast milk, is more desirable.

Levine and his associates,[22] after showing that premature infants could not properly metabolize tyrosine and phenylalanine without ascorbic acid, produced the same metabolic defect in full-term infants by feeding them these acids, and abolished it by adding ascorbic acid to this diet. As previously noted, they suggested that the need for ascorbic acid might be increased as the protein of the diet was increased. This may well be the explanation of the seeming increased need of artificially-fed infants for the vitamin.

It is evident that the artificially-fed infant receives less ascorbic acid than his breast-fed colleague and that this ingestion is less effective either because of less efficient utilization of the vitamin or a greater need for it. The possibility of a deficiency of ascorbic acid in the artificially-fed infant is not unlikely.

It is not necessary to review here the vast literature dealing with the relation of ascorbic acid deficiency to decreased resistance to respiratory infection. It is suggested that this vitamin may also be one of the substances contained in human milk which enhances the breast-fed infant's resistance to respiratory infections.

Because ascorbic acid has such varied functions to perform in the infant's body, it is difficult to estimate the daily requirement by any single test. Selleg wrote,[37] "It seems evident that the normal requirement of vitamin C per day for an infant may be estimated from the amount supplied in mother's milk when the parent is receiving a good diet." Snelling's work[20] shows that 30 mg. per day were not sufficient to raise the ascorbic acid plasma level of the artificially-fed infant to that of the breast-fed baby; and Mindlin's work[36] shows that even 75 mg. of the vitamin per day were not sufficient to accomplish this. Bakwin[38] reported that it required 75 to 100 mg. of ascorbic acid daily to keep the blood level of the artificially-fed infant comparable to that of the breast-fed infant. It would seem reasonable to allow the artificially-fed infant at least 100 mg. of ascorbic acid per day, to administer this in divided doses in each feeding and to begin such administration as soon as the infant begins to take food by mouth.

SUMMARY

1. Breast feeding in infancy is natural and preferred when practical and feasible.

2. The great majority of all infection in infancy is respiratory.

3. The only valid objection to the proper artificial feeding of infants would seem to be the resulting higher incidence of respiratory infections during the second half year of life, amounting to 1.43 respiratory infections per artificially-fed infant and 0.95 respiratory infections per breast-fed infant.

4. It would seem that the breast-fed infant's greater resistance to respiratory infections arises from some substance or substances contained in human milk.

5. There is no significant difference in the amount of diarrhea and miscellaneous infections between babies breast- and properly artificially-fed.

6. The high incidence of diarrhea in partially breast-fed infants may result from attempts to have an unwilling mother breast feed her baby.

7. The vitamin A daily intake of the 6-month-old, breast-fed infant approximates 3,250 I. U. as compared with the daily 1,500 I. U. recommended by the Food and Nutrition Board of the National Research Council. There is evidence to suggest that the infant's need for this vitamin is great and some evidence which suggests that he absorbs it more completely when he is breast-fed.

8. The ascorbic acid daily intake of the 6-month-old breast-fed infant approximates 55 mg. as compared with the daily 30 mg. recommended by the Food and Nutrition Board of the National Research Council. There is considerable evidence that the infant's need for this vitamin is great and that he absorbs it more adequately or needs it less when he is breast-fed.

9. Vitamin A and ascorbic acid may be the substances that are stored by the breast-fed infant in quantities such as to give him greater resistance to respiratory infections in his second half year of life.

10. It seems reasonable to offer the artificially-fed infant vitamin A and ascorbic acid in quantities at least as great as he would receive if he were breast-fed and to include these in the diet of the first days of life. Two hundred and twenty I. U. of vitamin A per pound of body weight, and 100 mg. of ascorbic acid in divided doses, are suggested as daily allowances.

11. It is hoped that the artificially-fed infant who receives adequate amounts of vitamin A and ascorbic acid will possess resistance to respiratory infections equal to that of the breast-fed baby.

CONCLUSIONS

It is natural and preferable to feed an infant at his mother's breast. If this is not practical, artificial feeding with cow's milk offers an adequate alternative. When the latter is carried out properly from all the standpoints which have been discussed, it seems to possess only one obvious disadvantage: the artificially-fed infant suffers from more respiratory infections during his second half year of life than does the breast-fed baby.

The notable difference between the dietary of the breast- and artificially-fed infant lies in the fact that the breast-fed baby receives more vitamin A and ascorbic acid and seems to utilize these vitamins better or to have less need of them. The Recommended Dietary Allowances for these vitamins of the Food and Nutrition Board of the National Research Council, as suggested for the 6- to 8-month-old infant, are low when compared to the amounts of them which the breast-fed infant receives.

It seems reasonable to allow the artificially-fed infant, beginning in the first days of life, 220 I. U. of vitamin A per pound of body weight daily, and 100 mg. of ascorbic acid daily offered in several divided doses, in the hope that this may lessen the incidence of respiratory infections which he suffers in his second half year of life.

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REFERENCES

1. Scevola de Sainte-Marthé: La Paedotrophia, or The Art of Bringing Up Children, 1584: translated from the Latin by H. W. Tytler, London, 1797; quoted in Pediatrics of the Past, compiled by John Ruhrah (New York, 1925, Paul B. Hoeber, Inc., p. 508); quoted in Poet Physicians, compiled by Mary Lou McDonough (Springfield, Ill., 1945, Charles C Thomas, p. 11). Used by permission of both publishers.
2. Mueller, A. J. and Cox, W. M., Jr.: Comparative Nutritive Value of Casein and Lactalbumin for Man, Science **105**: 580, 1947.
3. Gordon, H. H., Levine, S. Z., and McNamara, H.: Feeding of Premature Infants, Am. J. Dis. Child. **73**: 442, 1947.
4. Stearns, G.: The Mineral Metabolism of Normal Infants, Physiol. Rev. **19**: 415, 1939.
5. Holt, L. E. Jr., Tidwell, H. C., Kirk, C. K., Cross, D. M., and Neale, S.: Studies in Fat Metabolism I. Fat Absorption in Normal Infants, J. PEDIAT. **6**: 427, 1935.
6. Powers, G. F.: Infant Feeding, J. A. M. A. **105**: 753, 1935.
7. Grulee, C. G., Sanford, H. N., and Herron, P. H.: Breast and Artificial Feeding, J. A. M. A. **103**: 735, 1934.

8. Grulee, C. G., Sanford, H. N., and Schwarz, H.: Breast and Artificially Fed Infants, J. A. M. A. **104**: 1986, 1935.
9. Ebbs, J. H., and Mulligan, F.: The Incidence and Mortality of Breast- and Artificially-Fed Infants Admitted to Hospital with Infections, Arch. Dis. Child. **17**: 217, 1942.
10. Stuart, H. C. and Staff: Studies from The Center for Research in Child Health and Development, School of Public Health, Harvard University. I. The Center, the Group Under Observation, Sources of Information, and Studies in Progress. Monographs of the Society for Research in Child Development IV: Serial 20, No. 1, 1939.
11. Teel, H. M., Burke, B. S., and Draper, R.: Vitamin C in Human Pregnancy and Lactation 1. Studies During Pregnancy, Am. J. Dis. Child. **56**: 1004, 1938.
12. Mindlin, R. L.: Variation in the Concentration of Ascorbic Acid in the Plasma of the Newborn Infant. J. PEDIAT. **16**: 275, 1940.
13. Braestrup, P. W.: Studies of Latent Scurvy in Infants II. Content of Ascorbic (cevitamic) Acid in the Blood-Serum of Women in Labour and in Children at Birth, Acta Paediat. **19**: 328, 1937.
14. Byrn, J. N., and Eastman, N. J.: Vitamin A Levels in Maternal and Fetal Blood Plasma, Bull. Johns Hopkins Hosp. **73**: 132, 1943.
15. Lewis, J. M., Bodansky, O., Lillienfeld, M. C. C., and Schneider, H.: Supplements of Vitamin A and of Carotene During Pregnancy, Am. J. Dis. Child. **73**: 143, 1947.
16. Dann, W. J.: The Transmission of Vitamin A from Parents to Young in Mammals, Biochem. J. **26**: 1072, 1932.
17. Sargent, F. II., Lombard, O. M., and Sargent, V. W.: Further Studies on Stability of Resistance to the Common Cold, Am. J. Hyg. **45**: 29, 1947.
18. Lawrence, J. M., Herrington, B. L, and Maynard, L. A.: Human Milk Studies: XXVII, Comparative Values of Bovine and Human Milks in Infant Feeding, Am. J. Dis. Child. **70**: 193, 1945.
19. Recommended Dietary Allowances, Food and Nutrition Board, National Research Council, revised 1945.
20. Snelling, C. E.: The Plasma Ascorbic Acid of Infants and Children, J. PEDIAT. **15**: 824, 1939.
21. Dann, M.: The Influence of Diet on the Ascorbic Acid Requirement of Premature Infants, J. Clin. Investigation **21**: 139, 1942.
22. Levine, S. Z., Gordon, H. H., and Marples, E.: A Defect in the Metabolism of Tyrosine and Phenylalanine in Premature Infants, J. Clin. Investigation **20**: 209, 1941.
23. Daniels, A. L.: Vitamin A Content of Fecal Excretion of a Breast-Fed and Artificially-Fed Infant, Preliminary Report, Proc. Soc. Exper. Biol. & Med. **23**: 824, 1926.
24. Bloch, C. E.: Blindness and Other Diseases in Children Arising From Deficient Nutrition (Lack of Fat Soluble A Factor), Am. J. Dis. Child. **27**: 139, 1924.
25. Boynton, L. C., and Bradford, W. L.: Effect of Vitamins A and D on Resistance to Infection, J. Nutrition **4**: 323, 1931.
26. Lewis, J. M., Bodansky, O. and Shapiro, L. M.: Regulation of Level of Vitamin A in Blood of Newborn Infants, Am. J. Dis. Child. **66**: 503, 1943.
27. Ellison, J. B. and Moore, T.: The Vitamin A Reserves of the Human Infant and Child in Health and Disease, J. Soc. Chem. Industry **55**: 236, 1936.
28. Wolff, L. K.: On the Quantity of Vitamin A Present in the Human Liver, Lancet **2**: 617, 1932.
29. Rowntree, J. I.: A Study of the Absorption and Retention of Vitamin A in Young Children, J. Nutrition **3**: 265, 1930.
30. Lesher, M., Brody, J. K., Williams, H. H., and Macy, I. C.: Human Milk Studies XXVI: Vitamin A and Carotenoid Contents of Colostrum and Mature Human Milk, Am. J. Dis. Child. **70**: 182, 1945.
31. Lewis, J. M., Bodansky, O., and Haig, C. Level of Vitamin A in the Blood as an Index of Vitamin A Deficiency in Infants and Children, Am. J. Dis. Child. **62**: 1129, 1941.
32. May, C. D., Blackfan, K. D., McCreary, J. F., Allen, F. H. Jr.: Clinical Studies of Vitamin A in Infants and Children, Am. J. Dis. Child. **59**: 1167, 1940.
33. Daniels, A. L., Armstrong, M. E., and Hutton, M. K.: Nasal Sinusitis Produced by Diets Deficient in Fat-soluble A Vitamin, J. A. M. A. **81**: 828, 1923.
34. Clausen, S. W.: The Effects of Moderate Deficiency of Vitamins, Bull. New York Acad. Med. **10**: 471, 1934.
35. Neuweiler, W.: Versuche über den Vitamin C Stoffwechsel beim Fetus, Klin. Wchnschr. **14**: 1040, 1935.
36. Mindlin, R. L.: The Relation Between Plasma Ascorbic Acid Concentration and Diet in the Newton Infant, J. PEDIAT. **13**: 309, 1938.
37. Selleg, I., and King, C. G.: The Vitamin "C" Content of Human Milk and Its Variation With Diet, J. Nutrition **11**: 599, 1936.
38. Bakwin, H.: Vitamin C Requirement of Infants, Report read before Acad. of Pediat. Region I Meeting, New York, June 1-3, 1939.

OBSERVATIONS ON INSECT-BORNE DISEASES IN THE SOUTH PACIFIC CAMPAIGN

PAUL HARPER, M.D.
BALTIMORE, MD.

THIS paper will review briefly the importance of insect-borne diseases to a military force in the tropics and will describe the joint Army-Navy organization which was developed in the South Pacific Area to control these diseases. This organization was as nearly a joint service group as was possible at the time and many of its virtues and accomplishments resulted from this combined service use of personnel and of supplies.

Whatever this organization accomplished was due to the efforts of many individuals too numerous to mention. However, it is proper here to acknowledge the noteworthy contribution of two Navy officers,* who have described the broad outlines of the problem[1] and the control program.[2] Also, the valuable work of nonmedical specialists, especially entomologists, parasitologists, sanitary and civil engineers should be emphasized. A more detailed account of the work of these various groups is given elsewhere.[3]

Insect-borne diseases were the most serious health hazard experienced by our forces in the South Pacific Area during World War II. Malaria was the most important of these diseases and attacked approximately 100,000 men during a period when our total force in the area was not much over twice this number. For a time malaria jeopardized the success of the military campaign. Dengue fever and filariasis were the other two most important diseases. On some bases and for short periods dengue fever became a more serious problem than was malaria. This disease appeared in epidemic form in 1943 on New Caledonia, Efate, Espiritu Santo, and Tulagi-Florida. On Santo it affected approximately 25 per cent of the base strength in an epidemic described by Stewart.[4] "Mumu," which is the native term for the early manifestations of filariasis, caused the evacuation of several thousand troops, mostly from the Samoan Islands. Scrub typhus was a localized but very real problem on Bougainville, in an epidemic described by Anderson and Wing.[5] The organization which was developed to control these insect-borne diseases at first was concerned primarily with malaria, and the story of this disease will serve to illustrate the entire program.

The geographical area with which this paper is concerned comprised the malarious islands of the South Pacific Area and especially the eleven islands which were the scene of extensive operations by our forces. This chain of islands lay north of New Zealand and northeast of Australia. Guadalcanal was about the center of the chain, which was stretched out over 1,500 miles of ocean. To

*Captain J. J. Sapero, M.C., U.S.N., the first area malariologist, and his successor, Commander Fred Butler, M.C., U.S.N.

[Editor's Note: For his work in the control of insect-borne diseases, Dr. Harper received the Mead-Johnson Award for 1945 from The American Academy of Pediatrics. See J. Pediat. 30: 742, 1947.]

the southeast of Guadalcanal were Espiritu Santo and Efate in the New Hebrides. To the northwest were Tulagi-Florida, the Russell Islands, the New Georgia Group, Vella La Vella, Treasure Island, Bougainville, Green Island, and Emiru Island, the latter two being in the Bismark Archipelago. This area is to be distinguished from the Southwest Pacific Area.

EARLY EPIDEMICS

The three factors which, in combination, resulted in the early and explosive epidemics of malaria were heavily infected natives, large numbers of anopheline mosquitoes, and susceptible troops. Each of these factors will be discussed briefly.

Table I shows malaria parasitemia rates among South Pacific natives. This table is a consolidated report of surveys on more than 11,000 natives, and shows an average parasitic index in the New Hebrides of 11 per cent and in the Solomons and the Bismark Archipelago of over 30 per cent.

TABLE I. MALARIA PARASITEMIA AMONG SOUTH PACIFIC NATIVES: CONSOLIDATED DATA FROM 71 SURVEYS

ISLAND GROUP	NO. SURVEYS	NO. EXAMINED	PARASITIC INDEX (%)	
			AVERAGE	RANGE
New Hebrides	18	8,000	11.5	5-57
Solomons	49	2,651	31.6	4-74
Bismarck Archipelago	4	663	32.0	12-48

Table II shows the relation of age to incidence of malaria parasitemia. Children under 5 years of age averaged over 91 per cent positive smears. Children from 6 to 15 years of age averaged about 66 per cent positive smears and individuals over 15 years of age averaged 29 per cent positive smears. The percentage of natives with splenomegaly ranged from 57 to 85. These data merely indicate the extent and seriousness of the seed bed of malaria in the native population.

TABLE II. RELATION OF AGE TO INCIDENCE OF MALARIA PARASITEMIA AMONG SOUTH PACIFIC NATIVES*

AGE GROUP† (YR.)	NO. SURVEYED	% POSITIVE	PLASMODIUM SPECIES (%)			
			VIVAX	FALCIPARUM	MALARIA	MIXED AND UNDETERMINED
0-5	163	91	54	15	13	17
6-15	220	66	58	19	6	16
Over 15	448	29	35	26	6	32

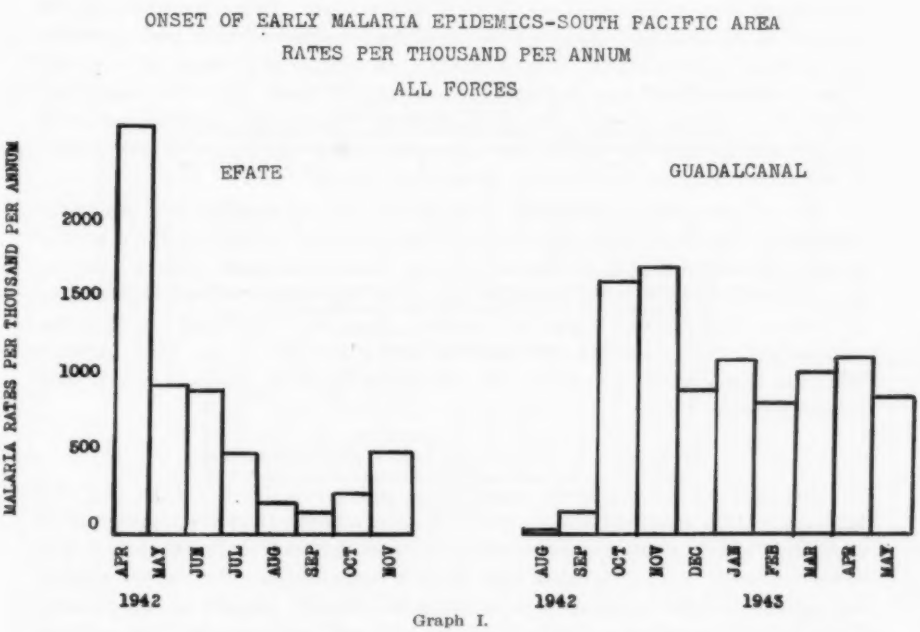
*Natives from Guadalcanal, Savo, Green, and Russell Islands.
†Ages are approximate.

The second factor in the early epidemics was the local vector, *Anopheles (Myzomyia) farauti*, Laveran, which has few if any equals as an effective and dangerous transmitter of malaria. This moquito and other local anophelines offered a particularly difficult problem in control because they would breed in so many types of water. They would lay eggs in fresh water, in brackish water, in clean water, in dirty water, in sunshine, and in light shade. Mos-

unhappily, they placed their eggs freely in road ruts and in shell holes. These man-made breeding places were estimated to account for more than 50 per cent of the mosquitoes on Guadalcanal. Mosquitoes breeding was aided by the high temperature and the heavy rainfall which averaged two to three times the rainfall which occurs along our north Atlantic seaboard.

Our troops fulfilled the last of the three conditions necessary for an epidemic. They were completely susceptible to all these insect-borne diseases.

Graph I shows the onset of the early malaria epidemics at Efate and at Gaudalcanal. A description of these epidemics will suffice to indicate the seriousness of the early situation.



Graph I.

Efate, in the New Hebrides Group, was occupied without opposition in March, 1942, by troops whose first task was to build an airfield. Their campsite was adjacent to the airfield and near a swamp and stream which later were discovered to be heavy breeding places of anopheline mosquitoes. Several hundred native laborers were encamped next to the troops and subsequently were found to be heavily seeded with malaria (Table I). Additional troops who were proceeding to a nonmalarious base and had their bed nets and other antimalaria supplies deep in the ship's hold, were diverted to Efate and landed early in April. The explosive outbreak of malaria which reached a rate of 2,678 per thousand per annum in April ensued from the close association of inadequately protected troops, infected natives, and anopheline mosquitoes.

Guadalcanal in the Solomon Islands, was occupied by amphibious assault on Aug. 7, 1942. Our troops who made the initial landings found few mosquitoes and had little malaria during the first weeks. No antimalaria work was done in this period. Meanwhile, anophelines were laying myriads of eggs in the fifty or more streams and lagoons and in the ruts and shell holes. Enormous mosquito populations were produced. A few cases of malaria appeared in August, more in September, and the disease became epidemic in October with a peak rate of 1,800 per thousand per annum in November. Epidemic rates continued for ten months.

It is difficult to realize the seriousness of the problem which was presented by these figures. One regimental surgeon on Guadalcanal reported that less than 50 per cent of his men were fit for active combat. In some outfits over 90 per cent of the men had malaria. Men had their chills and took their atabrine and quinine at their posts. Troops which were sent to rear areas for rest and rehabilitation suffered repeated malaria relapses and their return to combat was delayed for months beyond the expected date. The theater surgeon said that malaria was costing the theater the equivalent of two divisions in man power. It continued to exact this toll for more than a year.

The urgent military situation and the shortage of supplies were partially responsible for these early epidemics. It was necessary to occupy these islands months before the arrival of trained malaria control personnel over a year before adequate supplies were available, and at a time when atabrine was still an unfamiliar drug. The concept of "malaria discipline" had not yet been developed and the prevailing attitude was well expressed by one high ranking officer on Guadalcanal who said, "We are out to fight the Japs and to hell with the mosquitoes."

DEVELOPMENT OF MALARIA CONTROL ORGANIZATION

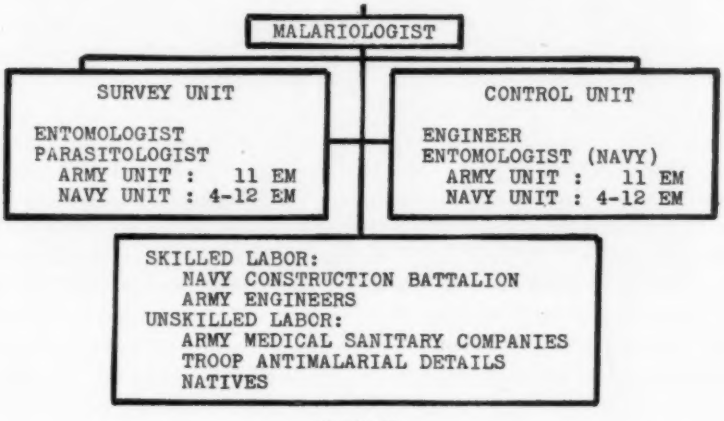
Graph II shows the basic organization which was developed to meet this situation. This basic malaria control group was responsible for insect control in an area of about twenty square miles and served 20,000 to 30,000 troops. The lower rectangle shows the labor part of this organization. The importance of one of these labor groups, the antimalarial details, should be emphasized. These details were formed in every company, and consisted of three enlisted men who were trained as will be described later and who were responsible for all insect control measures in the territory occupied by their company. Their chief work was to spray oil or a DDT mixture on all standing water in their camp area.

The technically trained group who were responsible to direct this work comprised the malariologist, the malaria survey unit, and malaria control unit. The survey unit consisted of an entomologist, and a parasitologist, and four to ten technicians. The entomologist and technicians provided information as to the kind of mosquitoes that were breeding, where they were breeding, and how they could be eliminated. The control unit comprised a sanitary engineer and eleven enlisted men, who directed the field control work which will be described

later. The engineer in command of the control unit was responsible for the work of most of the labor force shown in Graph II. Each engineer on the larger bases had from 100 to 250 men, exclusive of the antimalarial details, working under his general supervision. The malariologist was responsible for the coordination of the activities of all the persons in this organization.

It is to be emphasized that this group worked together as a team. Note that the personnel of the malaria control group could be either Army or Navy and that labor was also drawn from both services. On most islands the Army and Navy malaria control personnel lived in the same tents, ate at the same mess, and worked under a single malariologist.

BASIC GROUP
JOINT ARMY-NAVY MALARIA AND INSECT CONTROL
ORGANIZATION ON ISLAND BASES



Graph II.

One or more of the basic malaria control groups shown in Graph II were assigned to each island base according to the local needs. An island "Malaria and Epidemic Control Headquarters" was developed on Guadalcanal to coordinate the activities of the eight or more malaria control groups assigned there. Similar headquarters were set up on other large bases.

An important development was the attachment of such malaria control groups to combat divisions. These groups went ashore with the division and were responsible for the protection of combat troops from insect-borne diseases.

This whole organization was knit together by a small area headquarters consisting of a few Navy and Army Officers who had authority to travel throughout the area, and to inspect and recommend regarding the administration and coordination of malaria and epidemic control.

This organization began on Efate in July, 1942, with the arrival by air of one Navy officer (the first theater malariologist) and two enlisted technicians. Table III shows the size to which this organization had grown in the two years

TABLE III. MALARIA AND INSECT CONTROL PERSONNEL (MAY, 1944)

DESCRIPTION	NO.
Technically trained personnel (malariologists, malaria survey and control units)	771
Skilled labor (navy construction battalions and army engineers)	634
Unskilled labor (medical sanitary companies, troop antimalaria details, natives)	3,002
Total	4,407

following its establishment. There were over 700 technically trained personnel, over 600 skilled and 3,000 unskilled laborers working full time at insect control problems.

TRAINING AND EDUCATION PROGRAM

One of our major endeavors was a training and education program, which paid as great dividends per hour of effort as any other activity. This program was planned to reach every officer and man in the area on a level consistent with his responsibility.

An area training center for control of malaria and other insect-borne diseases was established and gave a two-week course for malariologists. An apprenticeship training program was developed for all newlyarrived malaria survey and control units and for malariologists. The apprenticed personnel worked in the field for several months with a veteran teaching group before undertaking independent responsibility. Schools were held for antimalarial details by every base malaria control group and gave a three-day course in field control methods which was attended by from 4,000 to 5,000 men over a two-year period.

A wide publicity and educational program to improve "malaria discipline" was undertaken. Posters, calendars, and comic strips featuring "Malaria Moe" and "Miss Anopheles" were prepared by our own artists, printed locally, and distributed widely. Pocket sized manuals were prepared on malaria and on a few other diseases and a copy given to every officer and man in the area.

SURVEY AND CONTROL MEASURES

No attempt will be made to describe survey and control measures in detail. A few activities will be described briefly and photographs will be used to illustrate some features of the work.

The parasitological section of the survey unit was responsible for all parasitological studies both on natives and on military personnel. Each large base had from several hundred to several thousand natives living within the troop area. Fig. 1 shows a blood smear survey of a native labor group on Guadalcanal. Note the typical open thatched type of construction. It would not have been feasible to screen these buildings even if screening had been available. The temporary solution was to give atabrine to these natives and to control rigidly all mosquito breeding near their village area. As soon as it was possible to build the necessary roads, all natives were moved to special camps which were located a mile away from the nearest troop quarters.

The entomological section of the survey unit was responsible for information about mosquitoes and other insects. During the early epidemics no one who observed the population of adult anopheline mosquitoes had any doubt about the inadequacy of control operations. Later, as control measures became more effective, it was rare to find adult anophelines within the occupied area. Then the entomologists developed an index of mosquito breeding based on a system of larval counts which were obtained by regularly dipping samples from all water catchments in the controlled area. Fig. 2 shows one of the field survey men looking for larvae in water which he has just dipped from a road rut. These larval counts became our best criteria of the success of control measures and any unusual breeding was immediately reported to the oiling details.

Fig. 1.—Blood smear survey in native labor camp on Guadalcanal. Note open thatched type of construction of hut.

Larval control measures were directed toward the elimination or reduction in the amount of water for mosquito breeding and to the application of oil and other larvicides to the remaining breeding areas. Ditching operations were the most important of the measures designed to reduce the size of water catchments. Native labor, working with machetes, was the most efficient means of clearing vegetation preliminary to ditching. The ditching was done by draglines, by dynamite and by hand labor, in that order. Fig. 3 shows a member of a company antimalarial detail using a knapsack sprayer in his company area.

Malaria was controlled by such methods as these for the first three years. DDT was not available until the fall of 1944; then it greatly facilitated control efforts.

Measures directed against adult mosquitoes included the use of bed nets, screening, repellents, and sprays of the pyrethin type until the introduction of DDT gave a powerful new attack. It was discovered that a single application of DDT sprayed onto a wood, canvas, or screen surface would have a so-called "residual-effect" which would kill mosquitoes and many other insects for the next three or four months. It was soon apparent that one of the most important uses of DDT was to spray the inside of native huts and of our own quarters for this residual action.

Fig. 4 shows a spray crew applying a coating of DDT dissolved in kerosene to the inside walls and screening of a mess hall. The kerosene evaporated and left the DDT in the form of fine crystals attached to wood and screen. These crystals of DDT were responsible for the residual effect and would kill all mosquitoes and flies which lighted on them for the next three months or more. This method promises to be one of the most effective means of controlling insect-borne diseases in the future, particularly under conditions of civil life.

Fig. 2.—Member of a malaria survey unit looking for anopheline larvae in water from a rutted area.

DDT made possible the efficient use of the airplane in larvicidal work. Early work was done with cub airplanes that carried about 25 gallons of DDT solution which was sufficient to spray fifty acres. The use of airplane spraying grew from these small beginnings, so that, by the end of the war, personnel from the South Pacific had set up on Okinawa an airplane-spraying program which was successfully larviciding about twenty-five square miles of rice paddies at weekly intervals, and was also used to reduce fly populations which would have reached enormous numbers unless checked. It should be emphasized that airplane spraying did not replace the hard work of ground crews but it did effectively supplement their efforts.

SUPPRESSIVE MEDICATION

A discussion of our experience with atabrine or quinacrine as it is now known cannot be presented here. Some of the field studies have been published by Downs[6] and by Schaffer and Lewis.[7] It may be summed up by saying that quinacrine was an extremely valuable tool in our work but that mosquito con-

trol was always the most important factor in malaria control. In fact, it was a theater policy to discontinue quinacrine suppression as soon as mosquito-control had reduced the transmission of malaria to a point where this was a safe procedure.

It is probable that the extremely low mortality rates and the rarity of blackwater fever was due to the wide use of suppressive atabrine. Over a two-year period, at the time when the incidence of malaria was at a peak, there were thirty-four deaths in more than 78,000 cases of malaria in army personnel, or a mortality rate of 0.0004. Atabrine was effective in suppressing both vivax and falciparum malaria, and had a curative action in the full sense of the word on the latter species.

Fig. 3.—Member of a company antimalarial detail using a knapsack sprayer.

RESULTS

One way to demonstrate the results of this insect control program will be to show graphs of malaria rates on a base occupied early in the campaign when there was no insect control organization as compared with the rates on a base occupied in the latter part of the campaign after the program had been well established.

The lower part of Graph III shows the malaria rates on Guadalcanal over a period of twenty-seven months. The upper graph shows the rates on Bougainville which was occupied fifteen months later. There was severe and prolonged combat on Bougainville and difficult problems of malaria control which were in many respects equivalent to those on Guadalcanal. But malaria control groups went ashore with each division, malaria discipline was good, supplies were adequate. The rates speak for themselves. Comparison of rates between divisions which arrived early in the campaign and those which arrived later show similar differences.

Fig. 4.—Application of a DDT spray for residual effect to inside walls and screen of a mess hall.

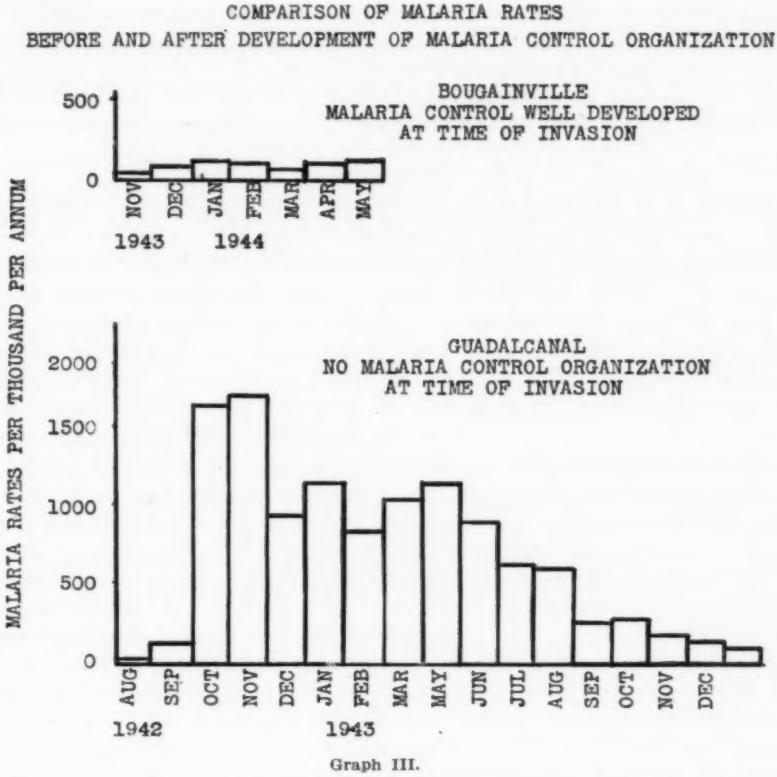
Effective control of dengue fever and of other insect-borne diseases also was obtained by this organization.[3, a and b]

COMMENT

The importance of observations such as these to the civilian community is worthy of comment. Malaria is the world's number one scourge. It accounts for 10 to 50 per cent of the cases of infectious diseases treated in hospitals or dispensaries in many of the countries of south and east Asia and of the East Indies.[8] It is estimated that over 100,000,000 cases of malaria occur each year in India, only about 10 per cent of which are treated. There are many back-

ward areas where there is little hope for lasting improvement in health or economy until this disease is conquered. Included in this category are the malarious islands of the South Pacific.

Two of the most immediately valuable developments of wartime research are DDT and the newer antimalarial drugs. One of the most interesting possibilities is the application of DDT residual spray to dwellings as the sole means of controlling malaria and dengue fever. This type of control was tried out with favorable results in the latter part of the war. DDT also was used to impregnate bed nets and preliminary tests indicated that this was a valuable procedure.



Graph III.

The shortage of quinine led to the wide use of and careful pharmacological study of atabrine and other drugs, notably chloroquin and paludrine. We now have drugs which in the case of faciparum malaria will exert a causal prophylactic effect and a cure in the full sense of the word. The problem of safe drugs with comparable action against vivax malaria remains.

SUMMARY

The hazard of insect-borne diseases, notably malaria, to military operations in the South Pacific Area from 1942-1945 is presented together with a brief description of the organization and methods which were successful in combatting the problem.

REFERENCES

1. Sapero, J. J., and Butler, F. A.: Highlights on Epidemic Disease Occurring in Military Forces in Early Phases of War in South Pacific, J. A. M. A. **127**: 502, 1945.
2. Butler, F. A.: Malaria Control Program in a South Pacific Base, U. S. Navy Med. Bul. **41**: 1603, 1943.
3. Malaria and Other Insect-Borne Diseases in the South Pacific Campaign, 1942-1945: Supplement to Am. J. Trop. Med. **27**: 1947.
   I. Harper et al.: General Aspects and Control Measures, p. 1.
   II. Downs et al.: Epidemiology of Insect-Borne Diseases in Army Troops, p. 69.
   III. Oman, P. W., and Christiansen, L. D.: Entomology, p. 92.
   IV. Levine, N. D., and Harper, P.: Parasitological Observations on Malaria in Natives and Troops, and Filariasis in Natives, p. 119.
4. Stewart, F. H.: Dengue: Analysis of Clinical Syndromes at a South Pacific Base, U.S.N. Med. Bul. **42**: 1283, 1944.
5. Anderson, W., and Wing, W.: Tsutsugamuchi Disease: A Study of Forty-nine Cases Occurring on Bougainville, War Med. **8**: 163, 1945.
6. Downs, W. G.: Results in an Infantry Regiment of Several Plans of Treatment for Vivax Malaria, Am. J. Trop. Med. **26**: 67, 1946.
7. Schaffer, A. J., and Lewis, R. A.: Atabrine Studies in the Field: I. The Relation of Serum Atabrine Level to Break Through of Previously Contracted Vivax Malaria, Bul. Johns Hopkins Hosp. **78**: 265, 1946.
8. Strong, R. P.: Stitt's Diagnosis, Prevention and Treatment of Tropical Diseases, The Blakiston Co., Philadelphia, p. 1.

WILMS' TUMOR (EMBRYOMA OF THE KIDNEY)

HENRY K. SILVER, M.D.
SAN FRANCISCO, CALIF.

WILMS' tumor (embryoma of the kidney) is a highly malignant tumor which originates in the kidney and is probably congenital. Patients with this tumor formerly were considered to have an extremely poor prognosis, but recent reports have shown that an appreciable number of patients will survive following nephrectomy and roentgen irradiation.

This report is based on a series of eighteen patients with Wilms' tumor of the kidney who were seen at the University of California Hospital between 1926 and 1944. The diagnoses in all cases were made by pathologic study of specimens obtained at operation or autopsy. Thirteen of these patients had a nephrectomy and ten of these are alive from two and one-fourth to at least fifteen years since treatment was instituted. (Table I).

DIAGNOSIS

Wilms' tumor is the most common abdominal neoplasm in children and almost all solid tumors of the kidney in early life are of this variety. The tumor characteristically grows very rapidly. However, Moore[1] has reported a case in a man aged 56 years, where a tumor was definitely known to be present for at least sixteen years, and in one of our patients (C. W.), aged 27 years, a mass in the abdomen was first noted 10 years before admission to the hospital. Metastasis takes place by direct extension or by way of the lymphatics or blood stream to other parts of the body, but in most patients the abdominal mass may became quite large before metastasis occurs.

There is a great variety and complexity of the microscopic findings in Wilms' tumor, and this great variation accounts in part for the multitude of names given to the neoplasm in the past: sarcoma, adenosarcoma, sarcocarcinoma, mixed tumor of the kidney, embryonal adenomyosarcoma, etc. Smooth and striated muscle cells, epithelial cells, and even bone and cartilage may be found in the tumor. Kretschmer[2] pointed out that all of the characteristic cell types usually are found if complete histologic studies are made of the tumors.

In most cases, Wilms' tumor appears before the age of 6 years, and fifteen of the eighteen patients in this series were less than 6 years old at the time of onset of their symptoms. Our youngest patient was only 3 days old when admitted to the hospital, and his mother had had difficulty in delivery because of the child's abdominal enlargement which had been produced by the tumor mass. Two of our patients were adults. The oldest was 27 years of age at the time of admission to the hospital, while another patient was 21 years of age. Eleven of the patients were females and seven were males.

The symptoms in this series of patients were similar to those reported by other authors. Abdominal enlargement or palpation of an abdominal mass was

From the Department of Pediatrics, University of California Medical School.

TABLE I. LIST OF SURVIVALS

PATIENT	AGE	SEX	TREATMENT	YEARS SURVIVAL
P. B.	5 mo.	F.	Nephrectomy	15
M. E.	4 yr.	F.	Nephrectomy; postoperative irradiation	11
C. W.	27 yr.	M.	Nephrectomy	10
R. C.	3 yr.	M.	Nephrectomy	9
D. E. B.	16 mo.	F.	Preoperative irradiation; nephrectomy; postoperative irradiation	7½
D. C.	18 mo.	F.	Nephrectomy; postoperative irradiation	6½
D. W.	10 yr.	F.	Preoperative irradiation; nephrectomy; postoperative irradiation	4½
L. M.	3 days	M.	Preoperative irradiation; nephrectomy; postoperative irradiation	4½
J. B.	21 mo.	M.	Nephrectomy; postoperative irradiation	2½
R. A. H.	3 yr.	F.	Preoperative irradiation; nephrectomy; postoperative irradiation	2½

the most frequent presenting sign. Abdominal bulging, when it occurred, was usually anteriorly and laterally, in contradistinction to tumors of the adrenal which may bulge posteriorly. Abdominal pain was present in almost one-half of these patients and in several instances it occurred before the abdominal mass had been noted. Urinary symptoms were infrequent and not significant. Gross hematuria was much less frequent than either abdominal mass or pain but it occurred in three of the patients during some time in their disease. In one case hematuria was observed before a definite abdominal mass could be palpated. Vomiting, anorexia, malaise, and weight loss were present in some patients but these symptoms were usually associated with a large tumor mass or occurred late in the course of the disease.

On physical examination, the most characteristic finding was an abdominal tumor mass which presented anteriorly or laterally, felt solid, was not tender, and usually had a smooth or finely nodular and rounded outline. In some patients the tumor occupied a large part of the abdominal cavity. The condition which gave the greatest difficulty in differential diagnosis was the neuroblastoma of the adrenal, but other conditions such as retroperitoneal sarcoma, polycystic kidney, hydronephrosis, lymphoma with marked enlargement of the liver or spleen, splenic or mesenteric cyst, ovarian tumor or cyst, and tuberculous peritonitis, should be considered. Since the hypernephroma or Grawitz tumor rarely occurs in early childhood, it should cause little difficulty in the differential diagnosis.

Of special interest in this series of cases was the presence of hypertension in seven out of eight patients in whom the blood pressure was recorded. The mechanism involved in the production of hypertension is not clear.[3] Bradley and Pincoffs[4] attributed the elevated pressure in patients with Wilms' tumor to the fact that the tumor tissue, like renal tissue, possessed the property of causing a rise in blood pressure. Horton[5] found that hypertension disappeared after removal of the primary tumor but that the blood pressure became elevated again when tumor metastases appeared. This would seem to support the possibility that some pressor substance, liberated by the tumor tissue, is responsible for the hypertension.

On the other hand, Koons and Ruch[6] have described a case of a 7-year-old girl with hypertension who was cured after nephrectomy in spite of the existence of metastases in other parts of the body. These authors suggested that the increase in blood pressure might be caused by interference with renal circulation when the renal pedicle has been invaded by the tumor tissue. Furthermore, they suggested that the neoplastic mass surrounding the kidney may act in the same manner as the cellophane envelopes used by Page[7] to produce experimental hypertension. Daniel[8] also studied the blood pressure in patients with Wilms' tumor and out of eighteen cases he found moderate or extreme elevation in fourteen instances. He was not able to demonstrate a pressor substance in the tumor tissue and he was of the opinion that renal ischemia, produced mechanically by the tumor, frequently accounted for the hypertension. He suggested that the persistence of the hypertension following nephrectomy might be due to sclerotic changes in the arteries of the other kidney which had been produced before operation by the prolonged arterial hypertension.

PYELOGRAPHY

Retrograde and intravenous or subcutaneous pyelography are of aid in diagnosing Wilms' tumor of the kidney. The tumor causes distortion of the renal pelvis and displacement of the kidney and ureter, and in some cases there is failure of visualization of the involved kidney pelvis. It has been pointed out that pyelography also has real merit in determining the presence and normality of the kidney of the opposite side and its use is indicated to determine the condition of the opposite kidney, even when there is little doubt concerning the diagnosis of Wilms' tumor.[9] Since retrograde pyelography requires general anesthesia and is a very traumatic procedure in male infants, subcutaneous or intravenous pyelography should be tried first. If these are not successful, and if pyelograms are necessary, cystoscopic examination is indicated.

BIOPSY

Aspiration biopsy was not attempted in any of the patients in this series, since it was felt that this procedure might dislodge malignant tumor cells into adjacent areas or set cells loose into the blood stream and thus increase the chances of metastases to some distant site. However, taking a biopsy is not necessarily associated with the early spread of metastases to other organs. One of our patients (R. A. H.) was operated for a suspected ruptured appendix and at operation a tumor of the kidney was found. Biopsy of the tumor mass was taken and after the diagnosis of Wilms' tumor was made she received a course of roentgen irradiation. A nephrectomy was done five weeks later and this was followed by another course of roentgen therapy. The patient is alive and well two and one-fourth years after the biopsy.

TREATMENT

Most authors agree that the best treatment of Wilms' tumor is nephrectomy plus roentgen irradiation. However, there is still considerable controversy

TABLE II. PATIENTS WITH

PATIENT	AGE	SEX	DATE OF ENTRY	FIRST SYMPTOMS	DURATION OF SYMPTOMS	TREAT PREOPERATIVE IRRADIATION
P. B.	5 mo.	F.	Oct. 1926	Abdominal pain	4 mo.	No
R. C.	3 yr.	M.	March 1927	Abdominal mass	1 week	No
P. F.	26 mo.	F.	Nov. 1927	Abdominal mass	2 weeks	No
L. C.	2 yr.	M.	March 1929	Anorexia	3 mo.	No
D. C.	18 mo.	F.	July 1931	Abdominal mass	5 mo.	No
M. E.	4 yr.	F.	Nov. 1932	Abdominal pain	4 mo.	No
C. W.	27 yr.	M.	Sept. 1934	a. Mass b. Polyuria	a. 10 yr. b. 6 mo.	No
R. E. H.	2 yr.	F.	July 1936	a. Poor wt. gain b. Hematuria	a. 6 mo. b. 4 mo. ago	No
M. K.	5 yr.	F.	Dec. 1936	Abdominal pain	3 mo.	No
I. J.	4 yr.	F.	July 1937	Poor appetite and fever	6 mo.	No
T. P.	21 yr.	M.	March 1938	Abdominal pain	2 mo.	No
D. E. B.	16 mo.	F.	March 1939	Poor wt. gain	4 mo.	Yes
J. C.	14 mo.	M.	Nov. 1939	Poor appetite	5 mo.	No
D. W.	10 yr.	F.	May 1942	Abdominal pain	6 weeks	Yes
L. M.	3 days	M.	June 1942	Abdominal mass	3 days	Yes
B. H.	2 yr.	F.	April 1943	Abdominal pain	6 mo.	No
J. B.	21 mo.	M.	Sept. 1944	Hematuria	1 week	No
R. A. H.	3 yr.	F.	Dec. 1944	Malaise	6 mo.	1. No 2. Yes

regarding the advisability of giving roentgen therapy before nephrectomy as well as after the tumor has been removed. Ladd and White[9] sponsor irradiation only after nephrectomy has been performed, since they believe that on a theoretical basis, preoperative roentgen therapy might facilitate the spread of metastases. They suggest that by eliminating preoperative irradiation and removing the tumor as soon as possible there would be less time and opportunity for metastases to take place to other parts of the body.

On the other hand, Priestly and Schulte[10] reported that they obtained their best results when nephrectomy was combined with both preoperative and postoperative roentgen therapy. Nesbit and Adams[11] have adopted the policy of reserving preoperative roentgen therapy for those cases in which the tumor is so large that operative removal would be very difficult technically. They recommend the use of postoperative irradiation in all patients.

WILMS' TUMOR OF THE KIDNEY

MENT	NEPHRECTOMY		POST-OPERATIVE IRRADIATION	BLOOD PRESSURE	COURSE		COMMENT
	DATE	TYPE OF INCISION					
No	Oct. 1926	Posterolumbar	No		Alive	at least 15 yr.	
No	March 1927	Posterolumbar	No	96/66	Alive	at least 9 yr.	Tumor adherent to surrounding structures at operation.
No	0	0	Yes		Dead		Biopsy and removal of part of tumor only.
No	0	0	No		Dead		At operation tumor considered inoperable.
No	Aug. 1931	Posterolumbar	Yes	118/90	Alive	at least 6½ yr.	
No	Nov. 1932	Posterolumbar	Yes		Alive	at least 11 yr.	
No	Sept. 1934	Posterolumbar	No	140/90	Alive	at least 10 yr.	
No	July 1936	Posterolumbar	No		Dead		Developed metastases to neck 4 mo. after operation.
No	0	0	No		Dead		Had pressure atrophy of liver.
No	July 1937	Posterolumbar	Yes		Dead		At operation retroperitoneal extension.
No	0	0	Yes	140/90	Dead		Biopsy only: tumor considered inoperable.
Yes	June 1939	Posterolumbar	Yes	130/100	Alive	7½ yr.	Prolonged bleeding time before operation.
No	Nov. 1939	Posterolumbar	Yes		Dead		At operation retroperitoneal extension.
Yes	June 1942	Transperitoneal	Yes	142/110	Alive	4½ yr.	Developed diabetes mellitus after operation.
Yes	July 1942	Transperitoneal	Yes		Alive	4½ yr.	Developed kyphosis after roentgen irradiation. Sibling died "cancer of kidney."
No	0	0	Yes	170/110	Dead		Biopsy only: tumor considered inoperable; metastases to liver.
No	Sept. 1944	Posterolumbar	Yes		Alive	2½ yr.	Pulmonary metastases 7 mo. after operation; treated with irradiation; alive 2 yr. later.
No Yes	1. Dec. 1944 2. March 1945	1. Biopsy 2. Transperitoneal	2. Yes	150/90	Alive	2¼ yr.	First operation for suspected appendicitis.

No standard treatment was used for the series of cases presented here. (Table II). Preoperative irradiation was first used by us in 1939 and since that time it has been employed chiefly in those patients in whom some technical difficulty was to be expected at operation. In one instance (B. H.) successful primary surgical removal of the tumor was impossible because of the extreme vascularity of the tumor mass and the presence of numerous friable veins. After roentgen therapy was given the patient was re-explored and it was found that there had been a marked decrease in the vascularity of the tumor. In this patient, at least, it was felt that preoperative irradiation would have increased the chances of survival by obliterating some of the blood vessels and permitting removal of the tumor mass at the time of the first operation.

The majority of patients in this series in whom a nephrectomy was done had their kidneys removed through a posterolumbar incision, but nephrectomy

through a transperitoneal approach has been used in several of our recent patients. From this small series no definite conclusion is possible regarding the best operative technique.

RESULTS AND PROGNOSIS

Ladd and White[9] summarized the literature on embryoma of the kidney in 1941 and they found thirty-eight probable cures out of 563 cases reported up to that time. The best series they noted were those of White,[12] who had two probable cures out of nine patients, Kretschmer,[2] with twenty-four cases and three cures, and Higgins and Shively,[13] who reported four survivals out of twenty-six patients. Ladd and White's series consisted of sixty operative cases with fourteen patients alive for at least two years, a survival rate of 23.3 per cent.

Since 1941, there have been a few more reports of comparatively large series of patients as well as several reports on the survival of one or two patients.[14] Weisel, Dockerty, and Priestley[15] have reported forty-two operated patients with seven patients alive from two to twenty years later. Dean[16] reported twenty patients with Wilms' tumor in whom irradiation was the only form of therapy, with five patients being alive five years later. However, it was not stated whether a pathologic diagnosis was made in all of these patients before therapy was started. Nesbit and Adams[11] had twelve patients in whom nephrectomy was performed and seven of them (58.4 per cent) were alive three and one-half to eleven and one-half years postoperatively. They also reported one patient with Wilms' tumor who had questionable chest metastases and was alive ten years after being treated with roentgen irradiation alone.

Our present series consists of eighteen patients with Wilms' tumor with ten survivals out of the thirteen patients who had a nephrectomy, a survival rate of 76.9 per cent.

It was not possible to trace any relationship between a particular symptom or sign and the outcome following adequate treatment. Both our oldest and youngest patient, aged 27 years and 3 days respectively, at the time of entry into the hospital, survived. There was no correlation noted in the group between age at onset and the end result. Only three of our patients had gross hematuria and all three of these patients survived. This is in contrast with the findings of Ladd and White, who noted that the ten patients in their series with this condition died. An elevated blood pressure before operation was not found to be a bad prognosis sign in our series since five of the seven patients with hypertension whose tumor were removed by nephrectomy are among those who are living.

One patient (J. B.) developed pulmonary metastases seven months after nephrectomy. He received roentgen irradiation to the involved area with rapid disappearance of the lesions, and he is alive and well more than two years later with no evidence of recurrence. Kerr[17] has reported the case of a 4-year-old girl who had pulmonary metastases which cleared after irradiation, and who was alive and well fifty-two months after treatment.

TABLE III. RESULTS OF NEPHRECTOMY FOR WILMS' TUMOR

TREATMENT	OUTCOME		SURVIVAL TIME OF LIVING PATIENTS
	ALIVE	DEAD	
Nephrectomy alone	3	1	15 yr., 10 yr., 9 yr.
Nephrectomy plus postoperative irradiation	3	2	11 yr., 6½ yr., 2½ yr.
Preoperative irradiation plus nephrectomy and postoperative irradiation	4	0	7½ yr., 4½ yr., 4½ yr., 2¼ yr.
Total	10	3	

The treatment used in the management of our patients varied considerably. Since preoperative roentgen therapy was first used in 1939, all of those who are alive more than seven and one-half years were treated by nephrectomy alone or by nephrectomy plus postoperative irradiation (Table III). All of those patients who had preoperative irradiation plus nephrectomy and postoperative irradiation are still alive. However, only four patients were treated by this method and it will be interesting to see whether this method of therapy will continue to give the best results.

SUMMARY AND CONCLUSIONS

1. A series of eighteen patients with Wilms' tumor of the kidney is presented. A nephrectomy was done in thirteen of these patients and ten of these are alive from two and one-fourth to fifteen years postoperatively, a survival rate of 76.9 per cent.

2. Two of the patients were adults, while the youngest patient was only 3 days old at the time of entry to the hospital.

3. Hypertension occurred in seven of the eight patients in whom the blood pressure was recorded.

4. No correlation was noted between age of onset, degree of hypertension, presence of hematuria, and the eventual outcome.

5. No standard treatment was used in the management of these patients, but all four patients who received preoperative irradiation plus nephrectomy and postoperative irradiation are alive.

6. Every patient who survived had had a nephrectomy.

7. The data available are insufficient to permit the evaluation of the merits of the transperitoneal as compared with the posterolateral approach to the kidney.

Sincere thanks for permission to report these cases are expressed to the Departments of Pediatrics, Surgery, Urology, Radiology, Pathology, and Medicine of the University of California Medical School.

REFERENCES

1. Moore, T.: A Mixed Tumor of the Kidney in an Adult, Brit. J. Surg. 30: 381, 1943.
2. Kretschmer, H. L.: Malignant Tumors of the Kidney in Children, J. Urol. 39: 350, 1938.
3. Braun-Menéndez, E., Fasciolo, J. C., Leloir, L. F., Muñoz, J. M., and Taquini, A. C.: Renal Hypertension, Springfield, Ill., 1946, Charles C. Thomas.
4. Bradley, J. E., and Pincoffs, M. C.: The Association of Adeno-myo-sarcoma of the Kidney (Wilms' Tumor) with Arterial Hypertension, Ann. Mt. Med. 11: 1613, 1938.

5. Horton, B. T.: The Relationship of Hypertension to Renal Neoplasm, Proc. Staff Meet., Mayo Clin. **15**: 472, 1940.
6. Koons, K. M., and Ruch, M. K.: Hypertension in a 7 Year Old Girl With Wilms' Tumor Relieved by Nephrectomy, J. A. M. A. **115**: 1097, 1940.
7. Page, I. H.: The Production of Persistent Arterial Hypertension by Cellophane Perinephritis, J. A. M. A. **113**: 2046, 1939.
8. Daniel, W. E.: The Hypertensive Factor in Wilms' Tumor, South. M. J. **32**: 1014, 1939.
9. Ladd, W. E., and White, R. R.: Embryoma of the Kidney (Wilms' Tumor), J. A. M. A. **117**: 1858, 1941.
10. Priestley, J. T., and Schulte, T. L.: The Treatment of Wilms' Tumor, J. Urol. **47**: 7, 1942.
11. Nesbit, R. M., and Adams, F. M.: Wilms' Tumor, J. PEDIAT. **29**: 295, 1946.
12. White, W. C.: Wilms' Mixed Tumor of the Kidney, Ann. Surg. **94**: 139, 1931.
13. Higgins, C. C., and Shively, F. L.: Malignant Renal Neoplasms in Children: Review of Twenty-Six Cases, Arch. Surg. **42**: 386, 1941.
14a. Ockerblad, N. F., and Carlson, H. E.: Wilms' Tumor: With Report of an Eight Year Cure, J. Urol. **50**: 265, 1943.
b. Daw, W. J.: Wilms' Tumor, Penn. M. J. **46**: 1293, 1943.
c. Rowe, E. W., and Frazer, M.D.: Roentgen Therapy of Wilms' Tumor, Radiology **42**: 107, 1944.
d. Sugarbaker, E. D.: An Application of Staging in the Removal of Difficult Wilms' Tumor, Ann. Surg. **120**: 901, 1944.
e. Mandeville, F. B., and Nelson, C. M.: Wilms' Tumor of Kidney with Five Year Survival Following Preoperative Roentgen Therapy and Nephrectomy, Urol. and Cutan. Rev. **49**: 204, 1945.
15. Weisel, W., Dockerty, M. B., and Priestley, J. T.: Wilms' Tumor of the Kidney: A Clinicopathologic Study of Forty-Four Proved Cases J. Urol. **50**: 399, 1943.
16. Dean, A. L.: Wilms' Tumor, New York State J. Med. **45**: 1213, 1945.
17. Kerr, H. D.: Treatment of Malignant Tumors of the Kidney in Children, J. A. M. A. **112**: 408, 1939.

ORAL PENICILLIN IN INFANTS

GEORGE S. HUSSON, M.D.
NEW YORK, N. Y.

THE obvious advantages of orally administered penicillin have attracted the attention of many workers, who have attempted to treat infections with this very effective antibiotic. Some of the early results were discouraging, but more recently, due to a clearer understanding of the factors involved in the administration of oral penicillin, this method holds great promise for the future in the treatment of infections caused by susceptible organisms.

McDermott and co-workers,[1] in 1945, demonstrated that penicillin given orally, using four to five times the intramuscular dose, produced adequate serum levels. In this study, it was also demonstrated that plain tap water was just as effective a vehicle as any other used (beeswax, antacids, etc.). Bunn and McDermott[2] treated forty-five cases of pneumococcus pneumonia and showed comparable results with oral penicillin as with intramuscular penicillin, if four to five times the intramuscular dose was given. Each patient was given a high initial dose orally, as was given when patients were treated with intramuscular penicillin.

Oberst[3] and associates showed that results obtained with oral penicillin combined with antacids were, on an average, similar to the results obtained when penicillin was administered in aqueous solution. Free, Parker, and Biro[4] in 1945, came to the same conclusion. Finland[5] also demonstrated that penicillin in saline gave as good levels as when given with buffer preparations. The doses administered were the usual intramuscular doses.

Seager's[6] results, however, demonstrated that oral penicillin was more effective in producing higher and more sustained levels when given with antacids than when it was given in tap water. Gyorgi[7] and associates, in 1946, in treating children ranging in age from 2 to 9 years, showed higher and more sustained levels with trisodium citrate-buffered penicillin than with penicillin in plain water.

Burke,[8] in 1945, and also Finland[5] in the same year, demonstrated higher serum levels when oral penicillin was given before meals. Libby,[9] in 1945, showed the advantage of administering oral penicillin before meals, and many other workers have agreed on the better levels obtained on the fasting stomach.

Henderson and McAdam,[10] in 1946, obtained high and sustained serum concentrations in infants to whom oral penicillin was administered experimentally. In infants under one month, with a dose of 100,000 units, bacteriostatic levels were obtained as long as fifteen hours after administration. With 10,000 units, bacteriostatic levels were obtained up to six hours. In nine infants ranging in age from one month to one year, 100,000 units produced adequate levels for six hours. Adequate levels in premature infants were obtained with a dos-

From the Department of Pediatrics, New York University College of Medicine and the Children's Medical Service, Bellevue Hospital.

age of 5,000 units. The penicillin in this report was given in the first ounce of a regular feeding. Buchanan[11] treated twenty-one infants with neonatal infections, using 4,000 units per pound of expected body weight per twenty-four hours orally in the first ½ ounce of a regular feeding. "Immediate striking results" were obtained. A few patients relapsed but responded to a second course.

From these reports it seemed possible that oral penicillin might find a place on an infant ward in the treatment of infections. This experimental study was undertaken therefore, to determine if penicillin is indeed absorbed from the alimentary tract of young infants and what blood levels may be expected.

PROCEDURE

The usual intramuscular dose of penicillin on the infant wards of this hospital is 5,000 to 10,000 units every three hours. It was decided to give two to four times this amount orally, and 20,000 units were given in one dose throughout this experiment.

The subjects used varied from one week of age to approximately 5 months. The weights ranged from 6 to 12 pounds. All the infants were free from infection.

Twenty-two determinations in all were made.

The penicillin was dissolved in water so that 20,000 units were contained in 5 to 10 c.c. of water. It was then put in a formula bottle and given to the infant and followed by a regular feeding.

At the start of the experiment, four serum levels were obtained at the following times; one-half, one, two, and three hours after the ingestion of the penicillin. This was later cut down to three levels taken at one, two, and three hours after administration of the drug, and it was finally cut to two serum determinations at one and three hours after ingestion of the penicillin. It was felt after the first six determinations, that information regarding blood levels was important at the end of the first and third hours. This materially reduced the technical work involved, yet still gave the information most desired. In five cases, because of the findings of Henderson and McAdam,[10] serum determinations were carried out at the end of four and six hours.

The method of penicillin assay used was the serial dilution method recommended by MacLeod[12] and used by the Army Air Forces. The test organism was the C-203 M.V. strain of Group A beta hemolytic streptococcus. The sensitivity of this organism was consistently found to be 0.015 units of penicillin per cubic centimeter. Sensitivity tests on the organism were done at weekly intervals.

Rammelkamp and Keefer,[13] in 1943 showed a sensitivity of hemolytic streptococcus to penicillin in a range from 0.019 to 0.156 units and most staphylococci were demonstrated to be sensitive to a penicillin concentration of 0.165 units per cubic centimeter or less. Meads[14] and his co-workers, in 1945, using a serial dilution method, did sensitivity studies on a great number of strains of the organisms found in the infections which are usually treated with

penicillin. The vast majority of the organisms tested were susceptible to a concentration of penicillin of 0.06 unit per cubic centimeter or less. A few resistant strains of meningococcus, staphylococcus and *Hemophilus hemolyticus* were reported in this study.

From the above data, an adequate therapeutic level of penicillin should be not less than 0.06 unit per cubic centimeter, unless the organism involved is tested and found to be more sensitive. In this study, therefore, levels of 0.060 unit of penicillin per cubic centimeter or over were considered adequate.

RESULTS

In all determinations made, up to and including three hours after ingestion, adequate therapeutic levels of penicillin in the serum were obtained.

In the six determinations made at the end of half an hour, five showed levels of 0.960 unit of penicillin per cubic centimeter. In levels taken at the end of one hour, seven out of twenty-two still showed a concentration of 0.960 unit per cubic centimeter. The lowest serum concentration at the end of one hour was 0.120 unit. This was in a 150-day-old, 10-pound Mongolian idiot (No. 21). In ten determinations taken at the end of two hours, levels ranging from 0.480 to 0.240 unit per cubic centimeter were obtained. In the three-hour determinations a maximum of 0.480 and a minimum of 0.060 unit of penicillin per cubic centimeter was obtained. The latter comparatively low level was in a 61-day-old, 10-pound infant (No. 16).

Five determinations were made four and six hours after the administration of oral penicillin. As can be seen in Table I, at the end of four hours, three

TABLE I. PENICILLIN SERUM LEVELS IN INFANTS FOLLOWING ORAL ADMINISTRATION

PATIENT	AGE (DAYS)	WEIGHT (LB.)	PENICILLIN LEVELS IN UNITS PER C.C.					
			½ HR.	1 HR.	2 HR.	4 HR.	3 HR.	6 HR.
1	6	7	--	0.240	--	0.480	--	--
2	8	6	--	0.960	--	0.480	--	--
3	11	7	0.960	0.960	0.480	0.240	--	--
4	12	7	0.480	0.480	0.240	0.240	--	--
5	14	7	0.960	0.480	0.240	0.240	--	--
6	16	8	--	0.480	--	0.240	--	--
7	20	6	0.960	0.960	0.480	0.240	--	--
8	22	6	--	0.960	--	0.240	--	--
9	30	8½	--	0.480	0.240	0.240	--	--
10	30	10	0.960	0.960	0.480	0.240	--	--
11	31	9	0.960	0.480	0.480	0.240	--	--
12	42	6½	--	0.480	0.240	0.240	--	--
13	49	6	--	0.480	0.480	0.480	--	--
14	50	7	--	0.480	0.240	0.240	--	--
15	58	8	--	0.240	--	0.480	--	--
16	61	10	--	0.480	--	0.060	0.060	0.000
17	62	11	--	0.960	--	0.480	--	--
18	64	7	--	0.480	--	0.240	0.015	0.000
19	83	8	--	0.240	--	0.120	0.120	0.000
20	103	12	--	0.480	--	0.120	0.015	0.000
21	150	10	--	0.120	--	0.120	--	--
22	153	12	--	0.960	--	0.120	0.015	0.000
Average	49	8	0.880	0.584	0.360	0.265	0.045	0.000

patients (No. 18, 20, and 22) showed levels which are considered therapeutically inadequate. One (No. 19) showed a high level of 0.120 units per cubic centimeter. This was an 83-day-old infant who had one and three-hour levels of 0.240 unit per cubic centimeter. At the end of six hours no penicillin was found in the serum of any of the five patients tested.

CURVE SHOWING AVERAGE AND INDIVIDUAL LEVELS

OF SERUM PENICILLIN CONCENTRATIONS

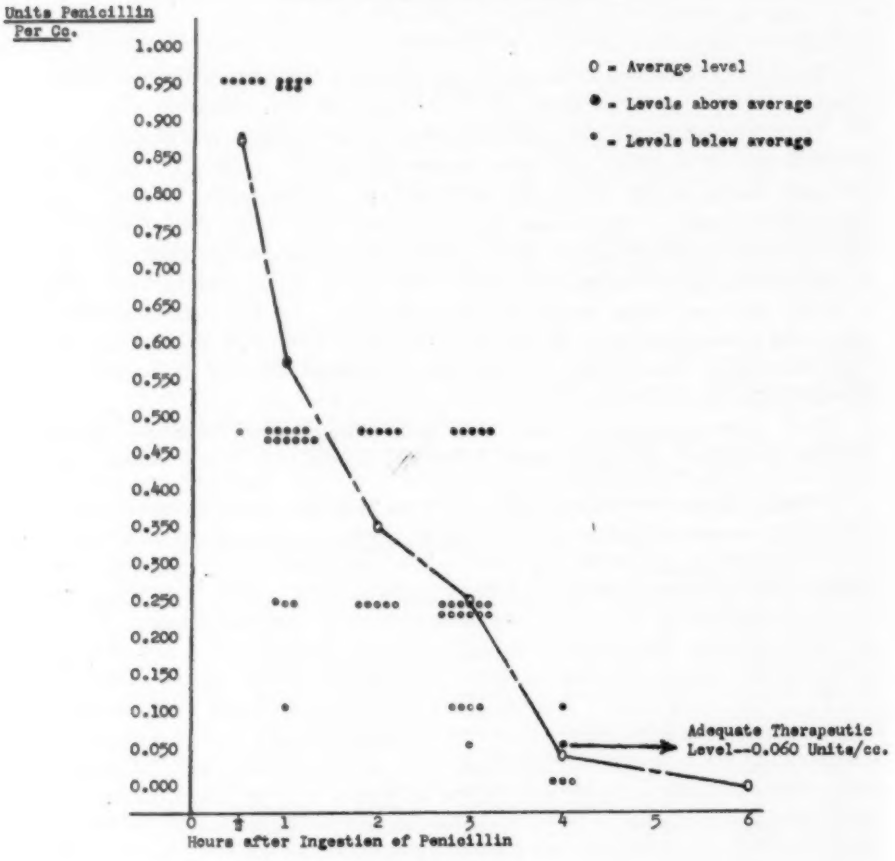


Fig. 1.

DISCUSSION

Although penicillin serum levels were not determined on adults or older children in this study, it seems clear that the levels obtained in young infants following oral administration are consistently higher than those generally found in older individuals. This difference may be due to several factors.

In 1941, Abraham and his associates[15] showed that oral penicillin was, to a great extent, destroyed by the acid content of gastric juice. The dosage range used was similar to that of intramuscular penicillin, namely 10,000 to 20,000 units. Rammelkamp and Keefer,[16] in 1943, substantiated Abraham's work and showed that gastric acidity was a definite factor in the inactivation of orally administered penicillin. In 1943, Rammelkamp and Helm,[17] using the same dosage as in intramuscular injections, and instilling the penicillin directly into the duodenum, obtained serum penicillin levels comparable to those obtained with intramuscular injection. Free, Parker, and Biro,[4] on the other hand, showed that gastric acidity is not so great an obstacle to oral penicillin administration as was originally believed. It was demonstrated by these workers that urinary penicillin excretion was the same whether penicillin was instilled directly into the duodenum or given by mouth to adults with acid gastric juice.

If the factor of gastric acidity is an obstacle to the absorption of ingested penicillin, it is much less so in the infant group. Miller[18] has shown that the maximum acidity of infant gastric secretions occurs during the first twenty-four hours of life, when it may reach adult levels. The theory offered to explain this phenomenon is that of placental transmission of maternal hormone (gastrin), which soon dissipates itself after the birth of the infant (Smith[19]). This acidity declines from birth until the tenth day of life, after which gastric acidity begins to rise again but never reaches adult levels until the third year. This was shown by both histologic and biochemical studies. Birth weight was shown to bear a direct relationship to gastric secretions, and achlorhydria was found quite frequently, especially in the lower birth weight groups. This factor may account in part for the high penicillin levels obtained in almost all determinations in this study.

The relative inefficiency of the infant kidney may be another factor of considerable importance in the production of the high sustained serum concentrations of orally administered penicillin. Using clearance studies on urea, inulin, sodium, and chlorides, McCance and Young[20, 20a] in 1937, demonstrated this relative inefficiency of the infant kidney. Gordon[21] and his associates also demonstrated the inefficiency of the infant and especially premature kidneys by urea clearance studies. Free[22] pointed out in 1944, that absorption of orally administered penicillin continues over a longer period than when it is given parenterally. Penicillin was also shown by Free to be rapidly excreted in the urine. The average amount of ingested penicillin which was excreted in the urine was between 10 and 33 per cent, and maximum urinary excretion occurred during the first hour after oral ingestion and fell off significantly thereafter. No penicillin was detectable at the end of six hours. An inefficient kidney would, therefore, seem to be an advantageous factor in the development of high penicillin levels initially and in the maintenance of high levels.

A third factor which may result in higher levels in the serum of young infants after receiving oral penicillin than is seen in adults ingesting comparable doses, is the possibility that there are fewer penicillinase-producing organisms in the infant gastrointestinal tract. Bunn and McDermott,[23] in 1946, demon-

strated that stool emulsions produced 80 to 100 per cent destruction of penicillin, whereas the same emulsion passed through a Seitz filter had no destructive action, thereby proving the inactivation of penicillin by penicillinase-producing organisms in the gastrointestinal tract. There is, however, no direct evidence that there are fewer penicillinase-producing organisms in the gastrointestinal tracts of young infants.

All twenty-two serum determinations in this study showed penicillin concentrations over and above levels necessary to inhibit the usual susceptible organisms up to and including three hours after administration. Penicillin administered orally would, therefore, seem to be a safe and practical method of treating infections in infants caused by the ordinarily penicillin-sensitive organism.

SUMMARY

1. Penicillin (20,000 units in water) was given to twenty-two infants ranging in age from one week to 5 months and ranging in weight from 6 to 12 pounds.

2. Serum levels were determined one-half, one, two, three, four, and six hours after ingestion of the penicillin.

3. At one-half hour, the average of six measurements was 0.880 unit per cubic centimeter. At one hour the average of twenty-two measurements was 0.584 unit per cubic centimeter. At two hours the average of ten measurements was 0.360 unit per cubic centimeter. At three hours the average of twenty-two measurements was 0.265 unit per cubic centimeter. At four hours the average of five measurements was 0.045 unit per cubic centimeter. At six hours no penicillin was found in the serum of the five infants tested.

4. All the levels up to and including three hours after ingestion were therapeutically adequate.

5. Some of the factors which might be involved in producing high, sustained levels in young infants after oral administration of penicillin are discussed.

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REFERENCES

1. McDermott, W., Bunn, P. A., Benoit, M., Dubois, R., and Haynes, R.: Oral Penicillin, Science **101**: 228, 1945.
2. Bunn, P. A., McDermott, W., Hadley, S. J., and Carter, A. C.: The Treatment of Pneumococcic Pneumonia With Orally Administered Penicillin, J. A. M. A. **129**: 320, 1945.
3. Oberst, F. W., Foter, M. J., and Nielson, F. A.: Blood Levels and Urinary Excretion after Oral Penicillin, J. Medicine **27**: 696, 1946.
4. Free, A. H., Parker, R. F., and Biro, B. E.: Oral Penicillin, a Comparison of Various Modes of Administration, Science **102**: 666, 1945.
5. Finland, M., Meads, M., and Ory, E. M.: Oral Penicillin, J. A. M. A. **129**: 315, 1945.
6. Seager, L. D.: Blood Levels of Penicillin after Oral Administration with Various Antacids, Science **103**: 353, 1946.
7. Gyorgi, R., Evans, K. W., Rose, E. K., Perlingiero, J. G., and Elias, W. F.: Oral Penicillin, Penn. Med. J. **49**: 409, 1946.
8. Burke, F. G., Ross, S., and Strauss, C.: Oral Administration of Penicillin, J. A. M. A. **128**: 83, 1945.

9. Libby, R. L.: Oral Administration of Penicillin in Oil, Science **101**: 178, 1945.
10. Henderson, J. L., and McAdam, I. W. J.: Oral Administration of Penicillin to Infants, Lancet **1**: 922, 1946.
11. Buchanan, J.: Penicillin in Infancy and Childhood, Lancet **2**: 560, 1946.
12. MacLeod, C.: Personal Communication.
13. Rammelkamp, C. H., and Keefer, C. S.: Penicillin and Its Antibacterial Action in Whole Blood and Serum for Hem. Strep. and Staph. Aureus, J. Clin. Investigation **22**: 649, 1943.
14. Meads, M., Ory, E. M., Wilcox, C., and Finland, M.: Penicillin Sensitivity of Strains of Six Common Pathogens and of Hemophilus Hemolyticus, J. Lab. and Clin. Med. **30**: 725, 1945.
15. Abraham, E. P., Florey, H. W., Chain, E., Fletcher, C. M., Gardner, A. D., Heatley, N. G., and Jennings, M. A.: Further Observations on Penicillin Lancet **2**: 177, 1941.
16. Rammelkamp, C. H., and Keefer, C. S.: Absorption, Excretion, and Distribution of Penicillin, J. Clin. Investigation **22**: 425, 1943.
17. Rammelkamp, C. H., and Helm, J. C.: Studies on Absorption of Penicillin from the Stomach, Proc. Soc. Exper. Biol. & Med. **54**: 324, 1943.
18. Miller, R. A.: Observations on Gastric Acidity During the First Month of Life, Arch. Dis. Child. **16**: 22, 1941.
19. Smith, Clement A.: Physiology of the Newborn Infant, Springfield, Ill., 1946, Charles C. Thomas.
20. McCance, R. A., and Young, W. F.: Secretion of Urine by Newborn Infants, J. Physiol. **99**: 265, 1941.
20A. Young, W. F., Hallum, J. L., and McCance, R. A.: Secretion of Urine by Premature Infants, Arch. Dis. Child. **16**: 243, 1941.
21. Gordon, H. H., Harrison, H. E., and McNamara, H.: Urea Clearance of Young Premature and Full Term Infants, J. Clin. Investigation **21**: 409, 1942.
22. Free, A. H., Leonards, J. R., McCullagh, D. R., and Biro, B. E.: Urinary Excretion after Oral Administration to Normal Human Subjects, Science **100**: 431, 1944.
23. McDermott, W., Bunn, P. A., Benoit, M., Dubois, R., and Reynolds, M. E.: Absorption of Orally Administered Penicillin, Science **103**: 359, 1946.

ORAL PENICILLIN IN THE PROPHYLAXIS OF RECURRENT RHEUMATIC FEVER

MARTIN M. MALINER, M.D., AND SOL DARRELL AMSTERDAM, M.D.
BROOKLYN, N. Y.

INNUMERABLE studies using sulphonamides as a prophylactic drug in recurrences of rheumatic fever have been reported. These varied from the earliest sulphanilamide through sulphadiazine and sulphamerazine. The Army and Navy, with vast numbers of individuals under control and observation, contributed much to the experimental evaluation of such chemoprophylactic measures.

Most of these studies are predicated upon the idea that the rheumatic disease occurs shortly after an upper respiratory infection due to certain types of the hemolytic streptococcus. The probable chain of events is: first, the initiating upper respiratory infection of one to three days' duration caused by particular hemolytic streptococci, followed by a latent interval of one to three weeks during which some phenomenon, either allergic, immunologic, or otherwise, takes place, subsequently followed by the clinical manifestations of the rheumatic infection in any of its protean forms.[1]

Holbrook[2] found as many as 50 per cent of certain susceptible persons had a recrudescence of rheumatic fever within two to three weeks following an upper respiratory infection. Hugh Morgan, in 1943, reported that "90 per cent of youths in World War II who suffered attacks of rheumatic fever while stationed in some army camps had an immediate previous streptococcus infection witih an average latent period of sixteen days before the symptoms of rheumatic fever developed."[3] Massel and Jones found, "At some army posts actual epidemics of rheumatic fever resulted when upper respiratory infections due to hemolytic streptococci were prevalent."[4]

According to Hansen, "The very characteristic feature of rheumatic fever is its tendency to occur in repeated episodes. The high mortality and morbidity are due to the recurrences of the infection; less than 1 per cent of the patients die during the initial attack, whereas 25-40 per cent die within 10-20 years following the onset. The large difference between the immediate and ultimate mortality may well be due to the tendency of this disease to strike in repeated episodes of rheumatic activity."[1]

The vast majority of individuals have more than one attack. Roth and coworkers[5] have found a 68 per cent recurrence rate in 488 children; Bland and Jones,[6] in 1,000 children found a 66 per cent recurrence rate and Wilson,[7] in 673 children, reports a recurrence rate of 85 per cent. In children Roth[5] finds that 73 per cent had a recrudescence within three years after the initial attack. The recent military experience indicates, however, that even many years may elapse before a recurrence appears.

From the Pediatric Cardiac Clinic of the Post-Graduate Medical School and Hospital of New York, N. Y.

The peak age for the onset of rheumatic fever is 6 to 8 years of age in contrast to the peak age from 11 to 13 years of age for the reactivation of the infection.[5] Wilson[8] observed that the likelihood of a recurrence before and after 16 years of age was 5:1.

With the above in mind, the authors believed that if the number of streptococcal sore throats could be reduced, the frequency of recurrences of rheumatic fever would be decreased.

Our observations took place at the Pediatric Cardiac Clinic of the New York Post-Graduate Hospital during the fall, winter, and spring seasons of 1945 to 1946 and 1946 to 1947. We used penicillin troches[9] as our prophylactic agent. The purpose of the experiment was to introduce the antibiotic at the actual site of the probable focus for the growth of the hemolytic streptococci, namely, the pharynx. We believe it would be more effective to have the therapeutic agent acting directly upon the focus of infection rather than to depend upon chemotherapeutic agents which require a definite blood level to achieve the necessary effect. An additional advantage with the use of penicillin over the sulpha drugs is that repeated leucocyte, hemoglobin, differential counts, and urine analysis are not required. Janet Baldwin[10] concludes in her recent report, "Despite our good fortune in not encountering serious toxic manifestations, it is to be emphasized that such should be watched for and that a total white cell and polymorphonuclear count should be followed for at least the first two months of the prophylactic therapy with the sulpha drugs. The urine should be followed for albumin and red cells at regular intervals throughout the treatment."

In our clinic in 1945 to 1946 we used lozenges of 1,000 oxford units of penicillin, and in 1946 to 1947 these were increased to 5,000 oxford units. The patients were advised to suck the troche slowly about one hour after each meal. A sufficient supply was distributed to last at first for two weeks, and was later increased to a month's supply, after which the patients were to report for their usual check-up. This was repeated during the fall, winter and spring months when the upper respiratory infections were most prevalent. A careful record of the cardiac, rheumatic, and symptomatic manifestations was charted at each visit.

For a preliminary study, as this one was, facilities for routine throat cultures before and after therapy were not available at that time. We feel, of course, that these procedures are important in an investigation of this kind and this will be done in a follow-up study. Levine and Hoyt[11] have reported an experiment which might shed some light as to the efficacy of local penicillin in the throat. Their subjects were told to chew on a paraffin base gum which incorporated 10,000 oxford units of penicillin. They took repeated saliva samples and found a level of 1.0 or more units per cubic centimeter saliva which persisted for over three hours. At three and one-half hours it dropped to less than 0.25 unit per cubic centimeter.

Rammelkamp and Keefer[12] found that 0.3 unit of penicillin is the upper limit needed for bacteriostasis of susceptible bacteria in plasma.

Forty-four children were under observation. Twenty-two received the penicillin troches and the others were followed as controls. During the first year of our experiment, these latter received parallel pellets of milk sugar as a placebo. This was discarded as unnecessary during the second year. In the penicillin group there were twelve boys and ten girls. In the control group there were eleven boys and eleven girls.

TABLE I

	AGE IN YEARS			
	1-3	4-6	7-10	11-13
Controls	1	3	10	8
Penicillin	0	1	7	14

	CARDIAC DIAGNOSIS			
	POSSIBLE HEART DISEASE	POTENTIAL (RHEUMATIC HISTORY)	RHEUMATIC (MITRAL DIS.)	CONGENITAL
Controls	3	7	8	4
Penicillin	2	4	11	4

Both control and penicillin cases had similar type histories and cardiac manifestations. The congenitals were included to ascertain the value of the drug in the prevention of subacute bacterial endocarditis.

OBSERVATIONS

We were not only interested in the question of rheumatic fever but also in learning the possible value of the penicillin in the prevention of so-called upper respiratory infections. Fifteen mothers, of the twenty-two patients receiving penicillin, stated that the general health of their children was much better and that they had fewer upper respiratory infections than prior to taking the penicillin and that when these did occur they were not severe. One mother stated that her child did do better in general, but that the child had frequent colds during both years under observation. Three children had frequent colds both winters. Two mothers were noncommittal and saw no improvement. These reports intimated that the troches were not a panacea and apparently did not prevent the common cold. None of the twenty-two patients receiving the penicillin lozenges developed rheumatic fever. In the control group, four children developed definite attacks of acute rheumatic fever. The following are the histories:

CASE REPORTS

CASE 1.—J. F., an 11-year-old white girl with a history of rheumatic polyarthritis and mitral insufficiency dating back to 1944, was sent to a convalescent cardiac institution where she remained for eighteen months. One year later in April, 1947, she developed a typical history of rheumatic fever beginning with an upper respiratory infection followed in two weeks by torticollis and chorea.

CASE 2.—S. P., an 8-year-old white girl, was first diagnosed as having rheumatic mitral insufficiency at the age of 4 years. She was free from any activity until March, 1947, when, following an upper respiratory infection, she developed joint pains, temperature, rapid pulse, and variations in the cardiac status. All laboratory data, including sedimentation rates, x-ray, and blood counts, corroborated the diagnosis of acute rheumatic fever.

CASE 3.—M. S., a 10-year-old white girl with yearly recurrences of chorea in 1943, 1944, and 1945 had a new attack of chorea in April, 1947. This patient's heart appears to be normal.

CASE 4.—J. Z., a 13-year-old white boy, was first hospitalized for rheumatic fever in 1943. At this time there was a carditis with complete heart block which cleared up and the patient was well until March, 1947, when an attack of polyarthritis occurred.

TABLE II. FINDINGS IN FOUR PATIENTS DEVELOPING RHEUMATIC ACTIVITY (NO PENICILLIN)

NAME	PRESENT DIAGNOSIS	FEVER	ARTHRITIS	TACHYCARDIA	NEW MURMURS	ELEVATED SED. RATE	PROLONGED P-R	INCREASED HEART SIZE	CHOREA
J. F.	R.H.D. M.I. Chorea	+	+	+	+	23,67	–	–	+
S. P.	R.H.D. M.I.	+	+	+	–	80,48,30	–	+	–
M. S.	Chorea	–	–	–	–	22	–	–	+
J. Z.	R.H.D. M.I.	+	+	+	–	47,30	–	–	–

SUMMARY AND CONCLUSION

We have reported our observations on forty-four children seen at the New York Post-Graduate Pediatric Cardiac Clinic. Twenty-two received penicillin troches prophylactically and the remaining twenty-two children were observed as controls without penicillin. None of the children receiving the penicillin prophylaxis developed signs of rheumatic activity, whereas four of twenty-two control cases presented definite attacks of rheumatic fever.

In conclusion, we cannot make any definite statements about the use of penicillin as a prophylactic measure in rheumatic fever, but we do feel that our results are very encouraging and warrant further detailed study. The possibilities for the use of penicillin as a prophylactic agent and its advantages over chemoprophylaxis are indicated. A more detailed study may definitely help to establish penicillin as the agent of choice in rheumatic fever prophylaxis.

REFERENCES

1. Hansen, A. E.: J. PEDIAT. 28: 296, 1946.
2. Holbrook, W. P.: J. A. M. A. 126: 84, 1944.
3. Morgan, H.: U. S. Dep't of Labor, Proc. Oct. 5, 1943, Children's Bureau pub. no. 308. 4: 1943.
4. Massell, B. F., and Jones, T. D.: Am. Heart J. 27: 575, 1944.
5. Roth, I. R. et al.: Am. Heart J. 13: 36, 1937.
6. Bland, E. F., and Jones, T. D.: J. A. M. A. 113: 1380, 1939.
7. Wilson, M. G.: Rheumatic Fever, New York, 1940, The Commonwealth Fund.
8. Wilson, M. D.: J. PEDIAT. 10: 456, 1937.
9. Penicillin Troches called Ledercillin (5000U.) furnished by the Lederle Laboratories, New York.
10. Baldwin, J.: J. PEDIAT. 30: 284, 1947.
11. Levine, M. G., and Hoyt, R. E.: J. A. Pharm. Ass. Scientific Ed. 35: 346, 1946.
12. Rammelkamp, C. H., and Keefer, C. S.: J. Clin. Investigation 22: 649, 1943.
13. Dodge, K., Baldwin, J. S., and Weber, M. W.: J. PEDIAT. 24: 483, 1944.
14. Kuttner, A. G., and Reyersbach, G. J.: Clin. Invest. 22: 77, 1943.
15. Hench, P., and Rosenblatt, E.: J. A. M. A. 132: 976, 1946.
16. Hench, P., and Rosenberg, E.: Med. Clin. N. A. 30: 489, 1946.
17. Coburn, A. F.: Am. J. Dis. Child. 70: 339, 1945.

CEREBRAL ABSCESS: A COMPLICATION OF CONGENITAL CARDIAC DISEASE (FALLOT'S TETRALOGY)

Report of Two Cases With Diagnosis and Operation

Alfred Hand, M.D.
Philadelphia, Pa.

THE boy whose history is given here and whose mother was told when he was 3 months old that he had a heart murmur, was 4½ years of age when first seen by me; cyanosis was moderate at times, all the distal phalanges were clubbed, the heart was enlarged, and there were several murmurs. One year later when I was called to see him he had an upper respiratory infection, nasal obstruction, headache, temperature of 101.2° F., and pulse of 105, the highest figures recorded in all the illness, the temperature ranging from 98° to 99.8° F., rarely 100.8° F., and the pulse coming down in a few days to 78, 66, 52, with a low of 48. The headache ceased on the third day when he seemed well, but it and the slight rise of fever returned on the fourth day and persisted. There was occasional purulent nasal discharge. Vomiting occurred a few times until the seventeenth day, when all food was rejected, and in the evening he had an attack of stiffening of the arms and legs, head held back, eyes rolled up, face white, and he screamed as if in sharp pain for twenty minutes, when he relaxed and wept for ten minutes. The next day examination showed pupils equal and reacting to light, no opisthotonos, knee jerks marked, ankle clonus distinct on right, slight on left, Babinski and Kernig negative, no evidence of otitis, and no vomiting. Another attack of stiffening the next day with pulse 48 and temperature 98° F., suggested Stokes-Adams' syndrome, so Dr. W. D. Stroud of the Children's Heart Hospital was called, the boy having another spastic attack as we entered the room. Dr. Stroud thought it did not resemble Stokes-Adams, attributing the bradycardia rather to intracranial pressure from either thrombosis, embolism, or abscess in the brain. Lumbar puncture was done on the twenty-first day taking 3 c.c. of clear fluid dropping at the normal rate. Eye-ground examination by Dr. Hunter Scarlett showed veins distended and very dark, disc outlines fuzzy, and the discs slightly swollen almost to 1 diopter. Radiologic examination of the head by Dr. Manges gave a negative result. The temperature was 98.2° F. but the blood count found a leucocytosis of 16,000. On the twenty-second day the right arm was not moved as much as the left, the tongue protruded to the right, and the right eye could not be abducted beyond the middle line. Dr. W. G. Spiller, the neurologist, confirmed the suspicion of brain abscess, left-sided, and the boy was at once taken to the Hospital of the University of Pennsylvania; where the brain-surgeon, Dr. Charles H. Frazier, trephined in the left temporal region, evacuating 42 c.c. of yellowish green,

Read at the meeting of the American Pediatric Society in Stockbridge, Mass., May 15, 1947.

turbid fluid of offensive odor; cultures showed no growth but smears revealed many polynuclears and gram-positive diplococci. The boy lived two days longer.

The thorough autopsy confirmed the clinical diagnosis of pulmonary stenosis with defect of the ventricular septum and hypertrophy of both ventricles (dextroposition of the aorta, as in Fallot's tetralogy, not being mentioned); there was thickening of the aortic and pulmonic valves and of the conus, suggesting chronic fibrous endocarditis, and on one of the aortic valves was a red vegetation 2 mm. in diameter; there was an acute esophagitis with purulent exudate unrecognized during life.

Dr. Frazier, after studying the brain with Dr. Winkelman, the neurologist, wrote down several points of interest: (1) the principal abscess (Fig. 1) had not ruptured into the ventricles; (2) there was not a well-defined abscess wall; (3) there was a second abscess in the occipital lobe on the same side and a similar focus of infection in the parietal lobe. Furthermore, there was no evidence of meningitis when the brain was removed nor was there any evidence of communication with the mastoid, middle ear, or any of the sinuses. It would seem, therefore, that possibly the abscesses, especially in view of their multiple character, were vascular in origin.

I witnessed the post-mortem examination and at my request the pathologist opened the mastoid cells through the inner plate, finding no inflammation at all.

None of us apparently thought of the two conditions of the heart and brain as being anything else than a coincidence, for no mention was made of any relationship between them. Speaking for myself, I had no such idea up to that time, but several years later, when looking through some of the early Transactions of the Society, read in the 1894 volume a paper by Dr. W. P. Northrup with the title "Congenital Pulmonary Stenosis (conus arteriosus): Incompleteness of Septum Ventriculorum: Cyanosis: Abscess of the Brain: Death at 4½ Years. (Specimen shown.)" And in the 1895 volume, Dr. George N. Acker, under the title "A Case of Cardiac Anomaly" reported the history of a girl 6 years old, developing an abscess in the right temporosphenoidal lobe; and following him, Dr. A. Jacobi read a paper "Patent Ventricular Septum in a Man of 29 Years." This patient also developed an abscess in the upper posterior part of the left temporosphenoidal lobe. Then, in the discussion of these papers, Dr. Frederic A. Packard told of a hospital patient who had been working up to two days before admission, showing Jacksonian epilepsy of the right arm but no cyanosis (when asked about it, he said he had never had it), the symptom getting worse, coma ensued, with death on the third day "the autopsy showing patent foramen ovale and a defect in the ventricular septum, each large enough to admit a finger, and the brain having an abscess." Dr. Packard did not mention the size nor the location of the abscess.

Five cases in all then gave the thought that there might be some reason for the association of these two distinct conditions, so a search was made through textbooks without avail. But about two years later, with the acquisition of an English work, *Diseases of Children*, edited by Garrod, Batten, Thursfield, and Paterson, and in consulting it while demonstrating to the Class in Pediatrics of

the Graduate Medical School of the University of Pennsylvania a patient with this type of congenital heart lesion, I found, in the chapter on "Diseases of the Heart," written by G. A. Sutherland, the statement, "It is an old-standing clinical observation that cases of congenital heart disease often suffered or died with signs of cerebral abscess or embolism. . . . It was recognized that venous thrombosis, septic or otherwise, was usually present in some other part of the body and it was assumed that some portion of the thrombus had been detached and passed into the blood-stream. The problem was as to how the embolus had passed through the lungs, which are the natural destination of a venous thrombus.

Fig. 1.—Case 1. Larger abscess in left temporosphenoidal region drained at operation; smaller abscess in left occipital lobe and third abscess in left parietal area not shown.

In these cases of paradoxical embolism there is present an opening in the ventricular septum and the embolus, passing through this, reaches the left ventricle and is then carried into the cerebral arteries. A similar explanation will hold good when there is a persistent foramen ovale or a patent ductus arteriosus."

At the meeting of the Medical Society of the State of Pennsylvania in 1940, Dr. Harold Krauss reported to the Pediatric Section abscess of the frontal lobe of otitic origin, and in the discussion it was agreed that the majority of cerebral abscesses in children are probably secondary to otitis or paranasal sinusitis, but I added that there is one class of pediatric patients who are specially susceptible to develop brain abscess from infection in any part of the body, the

congenital heart patients with septal defect, and that this should always be borne in mind in attending these patients. The explanation of this was followed by expressions of surprise on the faces of some members of the Section.

The next time that my attention was forcibly drawn to this subject was a year ago when my son showed me in one of his surgical journals an abstract of a very important article by Stanley L. Robbins (Arch. Int. Med. **75**: 279, 1945) who added three cases to the twenty-three mentioned in R. Hanna's paper,*

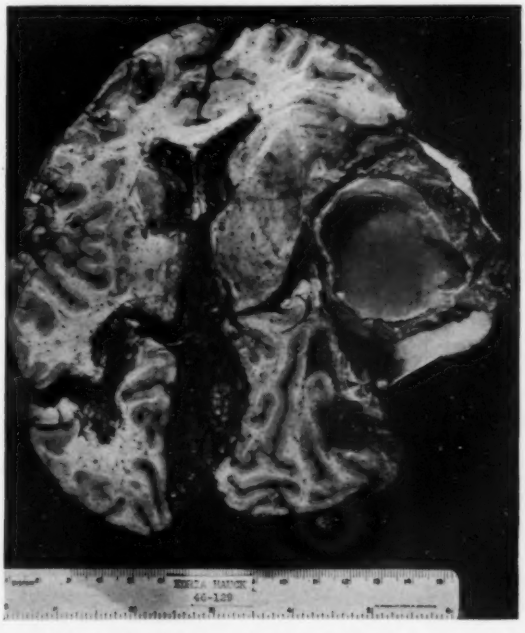

Fig. 2.—Case 2. Abscess in right occipital lobe drained, recovery following; six weeks after operation, symptoms of recurrence, exploration at site of operation negative, lumbar puncture showing general meningitis; autopsy showed large encapsulated abscess in right temporal lobe.

seventeen of them from the literature and six of Hanna's own. Dr. Robbins could find only three patients in which the abscess had been diagnosed during life and operated upon, one patient recovering. His comments are so pertinent and valuable that I quote them rather freely: "Brain abscess is a relatively unrecognized complication of congenital heart disease, so little known that only rarely does one find reference to it in any standard textbook of medicine. . . . In all probability, this apparent obscurity and paucity of reported cases represent the failure either of their recognition or of their publication rather than the rarity of their occurrence. . . . With the increased number of cases reported it is to be hoped that in patients with congenital heart disease, especially in those having the tetralogy of Fallot, underlying brain abscess will be considered in

*Am. J. Dis. Child. **62**: 553, 1941.

the diagnosis of any focal neurologic damage or meningitis. Certainly only early recognition will permit successful surgical intervention and hope for cure of this uncommon syndrome.

Fig. 3.—Case 2. Apex of heart to right, high liver shadow to left; autopsy showed left auricle and ventricle atrophic, the right being much hypertrophied and the heart practically bilocular; liver on the left, stomach, pancreas, and spleen on the right.

Dr. Robbins' comments impelled me to delve into notes of 20 years ago to place this case on record. A visit was made to the University Hospital to consult the autopsy records and Dr. Frazier's able successor, Dr. Francis C. Grant, on learning the object of the call, not only gave permission to inspect all the records, but also added the great and greatly appreciated favor of offering the notes of another case operated on recently in his department, to be included in this report. His patient, a girl 8 years of age, recovered after the operation, going home a month later, but was brought back after two weeks with fever, unconsciousness, and symptoms of a second abscess; the site of the first abscess was explored with negative results, but lumbar puncture showed acute meningitis and the patient succumbed after forty-eight hours. Autopsy disclosed a second abscess (Fig. 2)

encapsulated and filling the whole right temporal lobe. Also of interest in relation to the cardiac defects was a transposition of the viscera, recognized by radiology (Fig. 3) during life, the liver dome being on the left, the heart mainly on the right, autopsy showing the stomach, pancreas, and spleen on the right. The right ventricle and auricle were greatly hypertrophied while the left were so atrophic as to make the heart practically bilocular.

Another case in which the diagnosis of cerebral abscess was made during life with operation and recovery has been reported by one of our fellow members, Dr. Russell J. Blattner, in association with Drs. Edmund A. Smolik and Florence M. Heys* and this with the two added here gives a total of six operations with two recoveries.

Another case suspected but operation not permitted was observed by Commander Stanley S. Sidenberg, Lieutenant Colonel M. W. Kessler, and Major H. Wolpaw† in a boy 6 years old with a pulmonic systolic murmur, cyanosis, clubbing of fingertips, cardiac area not enlarged, and severe attacks of pain around the heart relieved by oxygen inhalations; a severe headache was followed two weeks later by sudden rise in temperature to 103° F. meningeal cry, rigid neck, spasticity of the right arm and leg, and death the next day. Examination post mortem showed many congenital anomalies, the main ones being Fallot's tetralogy and absence of the cerebellar vermis, with an abscess of the left parietal region, cultures giving *Staphylococcus aureus, Bacillus pyocyaneus* and *Bacillus coli.*

Since the reading of this paper, personal communications from two fellow practitioners, each having seen an unreported case (no operation during life) bring the total to thirty-six cases.

CONCLUSIONS

1. Reports of a total of thirty-six cases of congenital heart disease with abscess of the brain, found, without an exhaustive search, in the literature, when compared with the rather infrequent occurrence of congenital heart lesions in the average run of medical practice, justifies the belief that these patients, as a class, have greater susceptibility to this complication than all the other medical groups of children, even those with otitis or with acquired heart lesions.

2. Undoubtedly many cases are either unrecognized or unreported.

3. This susceptibility should receive greater attention in textbooks and in courses in the medical schools, especially in pediatrics, internal medicine, neurology, and surgery.

4. The parents and other caretakers of these patients should be told of this susceptibility and advised to watch in any acute illness for unusual symptoms that might be referred to the nervous system, such as facial neuralgia, or complaints of pain in any particular spot in addition to the ears, severe headache, general or localized, apparently causeless vomiting, muscular twitchings or loss of power, especially if of one side, and disturbances of vision.

*J. A. M. A. 130: 145-7, 1946.
†J. Pediat. 28: 719, 1946.

5. Those patients who live to be adults, as some do, should also be told, as tactfully as possible, that in any attack of acute illness, watch should be kept for any unusual symptom not felt before; a severe headache, twitchings of any muscles or loss of power, disturbance of vision, and such should be reported promptly to the doctor, in order that proper steps may be taken early; but that the patient should dismiss from his mind all thought of these as long as he is well.

6. All these patients in whom pulmonary stenosis, defect of the ventricular septum, coarction of the aorta, or patent ductus arteriosus is definitely proved or even suspected, should be examined by a surgeon especially trained in surgery of this closure of a patent ductus, or of anastomosis of the pulmonary artery with the aorta or one of its branches, or of excision of the narrowed aorta. The improvement in oxygenation following the operation of anastomosis undoubtedly favors improvement in the general health even if it may not lessen the possibility of paradoxical embolism. It is said of the operation for occlusion of the patent ductus arteriosus that it lessens the tendency to develop acute endarteritis or endocarditis which these patients are likely to show even in adult life, but it will certainly remove the possibility of brain abscess by paradoxical embolism. It would therefore seem to be strongly indicated in these ductus patients, unless there is some equally strong contraindication.

PERITONITIS ASSOCIATED WITH NEONATAL DIARRHEA

JOHN P. DOENGES, M.D.
BALTIMORE, MD.

THE three cases included in this paper present an unusual complication in a disease which commonly follows a quite characteristic pattern. Though neonatal diarrhea uniformly carries a grave prognosis, peritonitis secondary to rupture of an ulceration of the small bowel is rare in the experience of the staff of this hospital.

Two of the cases presented occurred during an epidemic of neonatal diarrhea. Seven infants between the ages of 1 and 10 weeks were involved in the epidemic. The clinical picture was similar in every case except for the terminal stages of two cases discussed in detail later in this paper. With each infant the stools were liquid, whitish green, foul smelling, and passed projectilely. Dehydration and acidosis closely paralleled the number and character of the bowel movements. Three of the infants recovered after intensive therapy. Four succumbed, and autopsies were performed in all of these cases. Two of these patients presented the typical post-mortem findings of dehydration, acidosis, and marasmus, and the other two deaths were due to peritonitis.

The third case presented in this paper was seen at Harriet Lane Home of the Johns Hopkins Hospital, and the clinical and pathologic findings were so similar to our cases that we have requested permission to include a brief abstract of it in our series. The case reports and pathologic findings in the three cases are as follows:

CASE 1.—A 3-week-old infant was admitted to the pediatric service Sept. 26, 1946, with the complaint of diarrhea of four days' duration.

This infant, born by cesarean section, Sept. 4, 1946, had a birth weight of 4 lb., 10 oz. Five days post partum she developed an impetigo over the groin, face, neck, and around the ears. Penicillin was given intramuscularly in doses of 3,000 units every three hours and penicillin ointment was applied locally to the lesions. A formula of Olac and water was started. The baby took this satisfactorily and improved rapidly. Weight on September 20, at time of discharge, was 5 lb., 10 ounces.

On September 22, the infant began to have diarrhea with several loose, greenish, squirting bowel movements. The formula was changed by the attending physician to boiled skimmed milk and water. The following day the stools became yellow in color, but remained liquid and became more frequent, so that the infant was having a movement every hour. Hospitalization was then advised.

Physical examination revealed a well-developed, white female infant, who apparently had recently lost weight. The infant was irritable and cried constantly. There was a diffuse, reddish, maculopapular rash, occasionally topped with a vesicle, over the face, neck, and chest. The skin was otherwise of normal color and texture. The fontanella were not depressed. Physical examination was otherwise negative. The temperature was 101°F.

From the Department of Pediatrics, Mercy Hospital Division of the University of Maryland School of Medicine.

Laboratory Results.—On September 26, urine examination was negative except for one plus actone. Microscopic examination showed 4 to 5 leucocytes per high power field. Blood count was: 94 per cent hemoglobin with 14.2 Gm.; 4.45 erythrocytes; 16,840 leucocytes with a differential count of 25 stab and 30 segmented cells, 44 lymphocytes and one monocyte with moderate toxic granulations. The carbon-dioxide combining power was 16 volumes per cent. Stool culture obtained on September 26 showed a growth of *Bacillus coli.* Stool examination was negative for blood ova and parasites. Stool cultures of September 30 and October 1, were negative for typhoid and dysentery groups. Complete blood examinations were made at about five-day intervals during the infant's hospital stay. The erythrocytes ranged between 3.91 and 4.98. The leucocyte count fell to 12,700 on September 30, then rose to 34,050 on October 7. On October 12, it was down to 18,400. The differential count remained essentially unchanged, showing a constant preponderance of the granulocytic series. However, on September 30, 8 eosinophiles were found to be present, and in succeeding counts the eosinophiles ranged between two and seven per 100 cells. On September 30, the blood sulfadiazine level was 15.1 mg. per cent. The carbon-dioxide combining power showed marked fluctations, corresponding to the degree of acidosis. On September 27, it was 40 volumes per cent; October 2, 36 volumes per cent; October 7, 26 volumes per cent; October 8, 8 volumes per cent; October 9, 5 volumes per cent; October 10, 33 volumes per cent; and October 12, 25 volumes per cent.

The baby was isolated on admission and started on ½ oz. of 5 per cent glucose by mouth every two hours. Forty cubic centimeters of plasma were given intravenously immediately and 200 c.c. of normal saline were given every three hours. On the evening of admission a formula was started containing evaporated milk diluted with molar lactate. On September 27, breast milk was started, and 1¼ oz. was given every three hours in ¾ oz. of boiled water. The breast milk was gradually increased as tolerated to 2½ oz. every three hours. On September 27, sulfadiazine, gr. 2½, was started and given every six hours. The infant received 50 c.c. of blood or 50 c.c. of plasma on alternate days throughout the remainder of her hospital course. Daily infusions of 150 c.c. of Ringer's lactate solution were given subcutaneously. The temperature remained elevated throughout the first week in the hospital, never going below 100°F. and with daily spikes as high as 103°F. Throughout this time the stools were liquid, yellow to whitish green, foul smelling and were expelled projectilely. The infant averaged nine to ten such stools every day. In spite of the number of stools, hydration seemed adequate and the skin rash cleared rapidly, so that by October 3, it had disappeared. She became distended on several occasions and on September 30 had two episodes of vomiting. However, enemas seemed to relieve the distention and the vomiting. Adequate vitamin therapy was given throughout the hospital stay. Between October 3 and October 8, the temperature gradually fell to a normal level under the above-outlined therapy but the infant continued to have between ten and fifteen liquid stools every day. The weight fell from 5 lb., 13 oz., on admission to 5 lb. on October 6. On October 9, the infant showed Kussmaul type of respirations and the carbon-dioxide combining power was 5 volumes per cent. Examination revealed a bilateral otitis media, and bilateral myringotomy was performed. Forty cubic centimeters of 5 per cent sodium bicarbonate were given intravenously. The respirations were slower and the child seemed improved; however, the stools did not change appreciably. Distention remained a problem. On October 13, the respirations became quite labored and in spite of oxygen therapy they ceased at 5:20 P.M.

Pathologic Report.—In the mesentery, numerous discrete, firm lymph glands were demonstrated. These were moderately enlarged and were seen throughout the mesentery up to its root. No enlargement of the lymph glands was demonstrated in the pelvis. Approximately two inches distal to the third part of the duodenum in the jejunum was a small segment of intestine, which appeared to be knuckled on itself, describing a horseshoe curve, so that a part of this knuckled loop appeared to be in contact with the other part.

Just above this area in the mesentery was a spot of whitish colored material, no larger than a drop or two, which looked like pus. When these two loops were dissected, there was in the proximal one a small area no larger than the head of a pencil, in which the serosa was

friable and necrosed in appearance. No free perforation was seen and no attempt was made to explore this area with an instrument for fear of creating one. None of the intestinal contents could be expressed from this necrosed area.

Microscopic Report.—The peritoneum had a very loose, edematous texture. There was an infiltration with polymorphonuclear cells, but no fibrin or exudate was encountered. The mucosa was uniformly and generally infiltrated with polymorphonuclear cells. Large areas showed necrosis of the mucosa. The infiltration was also seen in the submucosa and extended into the muscular wall. There were patches of fibrinous exudate on the serosal surface. There were no lymph follicles. Through the entire wall at one point extended a pool of polymorphonuclear cells. The muscle fibers were necrotic and the area suggested a point of perforation.

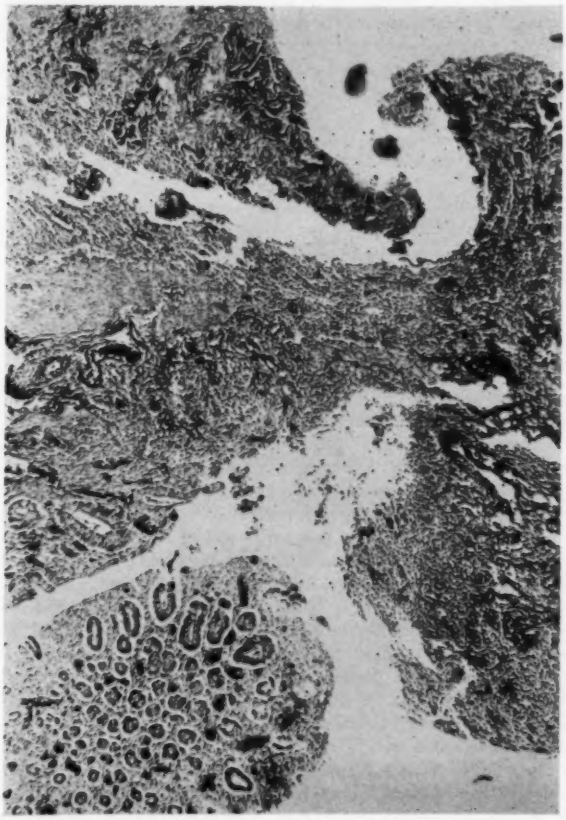

Fig. 1.—Photomicrograph through the ulceration described in the jejunum. Necrosis of the mucosa and submucosa with erosion is evident; there is marked cellular infiltration of the remaining strands of the muscularis (Case 1).

CASE 2.—A 3-week-old white male was admitted to the pediatric service on Sept. 22, 1946, with a complaint of diarrhea of four days' duration and a boil on the right buttock of two days' duration.

The child had been delivered normally at full term with low forceps. The hospital postpartum course had been uneventful and he was duly discharged. No details are recorded concerning the feeding of the child.

The mother stated that the child's stools were continually greenish since discharge from the hospital. On Sept. 8, 1946, the stools became more green than usual, watery, frequent (eight to twelve daily), but not foul. Two days later a purplish area developed on the right buttock which became inflamed. Diarrhea persisted, and hospital admission was sought.

On admission the temperature was 99.2° F., weight 7 lb., 13 oz. He was well developed, well nourished, crying, and in apparent distress. The fontanella were not depressed. The skin was of normal texture. Physical examination was negative except for a raised, red, warm area on the inner side of the right buttock. The abdomen was not distended, and showed no tenderness, rigidity, fluid, or masses.

Laboratory Results.—On admission urine examination was entirely normal. Blood count was: hemoglobin, 84 per cent with 12.6 Gm.; erythrocytes, 4.02; leucocytes, 12,700; differential, stab cells 17 per cent, segmented cells, 29 per cent, lymphocytes, 47 per cent, and monocytes, 7 per cent, with moderate toxic granulation. Subsequent findings were as follows: The urine occasionally showed a trace of albumin. There was a progressive anemia from a hemoglobin of 84 per cent, red blood cells, 4.02 on September 23, to a hemoglobin of 47 per cent, red blood cells, 2.43 on October 21. Granulocytes showed a shift to the left late in the hospital course with a differential on October 19, of premyelocytes, 1 per cent; myelocytes, 2 per cent; juvenile cells, 5 per cent; stab cells, 12 per cent; segmented cells, 4 per cent; lymphocytes, 69 per cent; and monocytes, 1 per cent. Turk cells and normoblasts were present in specimens of October 19 and 21. The white blood cell count on October 7 was 25,350; on October 12, 6,600; on October 19, 13,200; and on October 21, 4,300. Blood chemistry revealed blood chlorides, 367 mg. per cent; sodium chloride, 600 mg. per cent; urea, 35 mg. per cent; and urea nitrogen, 16 mg. per cent. The carbon-dioxide combining power was 21 volumes per cent on October 3 and 18 volumes per cent on October 21. Stool culture of September 26 was positive for *Bacillus coli*, but negative for the typhoid and dysentery groups. Stool cultures of September 27 and October 2 were negative for the typhoid and dysentery groups.

On admission the boil on the right buttocks was incised, and foul smelling pus was evacuated. After incision this lesion healed rapidly. Powdered lactic acid milk formula was given with adequate vitamin therapy. The child took all feedings hungrily, and retained all food. The stools continued being liquid or semiliquid, yellowish to greenish in color, and occasionally showed curds. There was a progressive weight loss to 6 lb., 11 oz. by October 9. From October 9 to 18 there was some slight increase in weight, so that on the latter date it was back to 7 lb. 7 oz. The temperature frequently spiked to 101° F. On October 3, respirations became accelerated and the abdomen somewhat distended. On October 5, the distention became a major problem and all feedings, except tea, were stopped. A cannula was inserted in the saphenous vein. M/6 Na-lactate, plasma, 5 per cent glucose, and whole blood were given. On October 6 a formula of boiled skimmed milk was started. Penicillin, 10,000 units, every three hours, was given. A half dram of Kaopectate was given every two hours. On October 10 the child refused the formula and became listless. A solution containing one Gm. of potassium chloride, 1.5 Gm. of sodium chloride, 20 c.c. of M-lactate, 355 c.c. of water, and enough glucose (5 per cent) to make 750 c.c., was given in 4 oz. feedings every four hours. Plasma and whole blood were given intravenously on alternate days. On October 12 the abdomen became quite distended and hard. A rectal tube and Pituitrin S brought no relief. On October 16 sulfadiazine was started. By October 21 abdominal distention was so pronounced that respirations became embarrassed. However, the temperature remained normal. On October 22 abdominal distention was tremendous. The child was irritable, respirations were labored, and there was regurgitation of fecal material. An enema returned yellow fecal material, but the distention was not relieved. The temperature was 101° F., pulse 128. Prostigmine was given without relief of distention. A constant rectal tube being ineffectual, a Wangensteen drainage was started. Continuous oxygen was given, but the respirations remained poor and ceased at 8:20 P.M.

Pathologic Report.—On opening the peritoneal cavity, a foul odor was noted. The loops of the bowel were matted together by lacy adhesions. Approximately 200 c.c. of yellow fluid was present. The bowel was markedly distended. The bowel wall appeared shiny. Strands

of fibrin were seen scattered over the intestinal wall. In the region of the cecum there was a walled-off pocket containing pus and fecal material. The walls were thin and ruptured easily. This abscess was approximately 2½ cm. in diameter. Between the loops of the small intestine there was a 2 cm. pocket of amber-colored fluid. The wall of this cyst was very thin and friable. There was marked lymphadenopathy of the mesenteric glands. The glands were firm, averaging ½ to 1 cm. in diameter and matted together. The omentum was included in the matting of the intestines.

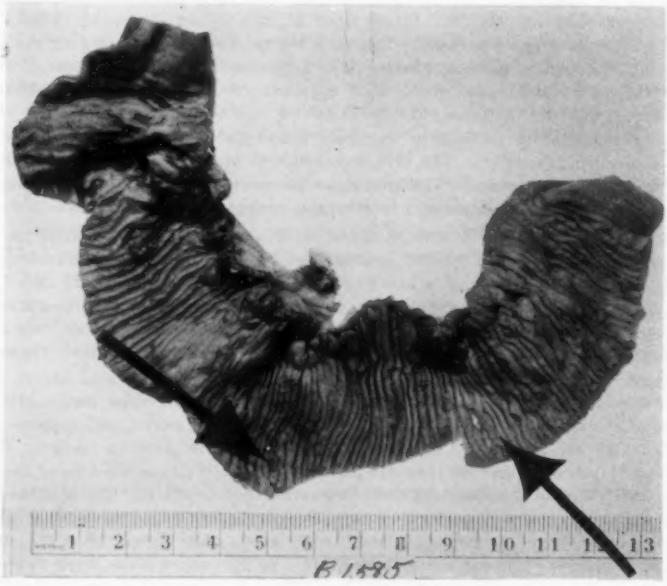

Fig. 2.—A specimen from the ileum showing numerous small ulcerations. The arrows indicate points of perforation (Case 2).

The stomach was distended. The mucosal pattern appeared normal. There were five small petechial hemorrhages on the mucosal surface of the greater curvature. The pylorus appeared normal. Throughout the entire small intestine there were multiple ulcerations measuring 1 mm. to 8 mm. in diameter. Each ulcer was surrounded by an area of induration measuring 1 mm. in width. On the serosal side of the bowel there was an area of hyperemia corresponding to each ulcer. Peyer's patches were enlarged and hyperemic. Two inches above the ileocecal valve there was an ulcer measuring 1½ cm. in diameter, which opened into the abscess cavity previously described. The entire bowel was very friable and was ruptured frequently during removal. The appendix was normal in size and position. The large bowel appeared entirely normal, showing no evidence of ulceration, hyperemia, or hemorrhage. The intestines contained much yellowish, curdy, fecal material and a moderate amount of mucus.

Microscopic Notes.—The entire thickness of the wall was diffusely infiltrated with polymorphonuclear cells, among which large macrophages were seen. There was also marked edema. The mucosa presented areas of interruption not typical of ulcers. These were merely segments of missing mucosa. There was not the usual granulation and fibrin surrounding these ulcerlike areas. The submucosa and wall of the bowel were infiltrated with leucocytes to the same degree as in the sections where the mucosa was intact. There was no evidence of coagulation or the development of a diphtheritic membrane. The peritoneal surface was covered with a fibrinous or purulent exudate. The Peyer's patches and solitary follicles were hypo-

plastic and difficult to differentiate. The mesenteric lymph nodes were edematous and infiltrated with polymorphonuclears. These showed no evidence of necrosis.

CASE 3.—This 17-day-old infant was admitted to Harriet Lane Home of the Johns Hopkins Hospital on October 30, 1946, because of diarrhea.

The baby was born at Provident Hospital, October 13, 1946, with a birth weight of 5 lb., 3 oz. The mother had pre-eclampsia, and labor was induced at thirty-one weeks. The baby was placed in an incubator and was given oxygen, as necessary, for listlessness and rapid respirations. Feedings consisted of Olac every three hours, but these were taken poorly and the baby steadily lost weight. On October 20, the infant developed thrush, and was treated with 1 per cent gentian violet. The baby began vomiting two days before admission and received 40 c.c. of 2½ per cent glucose daily because of this. At the time of admission, a loose, green, watery stool was noted. This apparently had not been present before. The temperature was 99.3° F., the pulse 90, respirations 28, and the weight 3 lb., 9 oz.

Physical examination revealed a markedly dehydrated, scrawny little infant who resembled a shrivelled premature. The skin was wrinkled and dry with turgor. The anterior fontanelle was slightly depressed. The buttocks were excoriated. The cry was hearty and the baby was alert. Physical examination was otherwise entirely negative.

Laboratory Results.—On October 30 the urine was cloudy, yellow, negative for albumin, and showed a one plus sugar without acetone; microscopic examination was negative. A blood study on October 30 revealed a hemoglobin of 22 Gm. The erythrocyte count was 5.25, leucocyte count 16,650, with a differential count of stab cells, 14; segmented cells, 24; lymphocytes, 54; and monocytes, 8. The red blood cells were hyperchromatic. On November 1, the hemoglobin was 22.5 Gm. The serologic test for syphillis was negative. On October 30 a stool culture showed a growth of pseudopyocyaneus.

After admission the infant continued to have watery, greenish-white stools. Thirty cubic centimeters of plasma were given intravenously and glucose and normal saline were given subcutaneously. Caffeine and sodium benzoate and adrenalin were given as needed. The infant was placed in an incubator and nothing was given by mouth. Fifty milligrams of ascorbic acid were given every day. On October 31 the temperature fell to 97° F. The child continued to have six to eight watery green stools every day. Repeated intravenous infusions of plasma and subcutaneous infusions of saline and glucose were given. On November 2 the infant was given 20 c.c. of glucose by mouth every three hours. By November 5 the stools appeared more formed and the child had only two on this day. The infant showed a constant weight gain, and on November 5 he weighed 4 lb. 5 oz. Ten cubic centimeters of skimmed milk were given every three hours.

On November 6 the temperature was elevated to 100.4° F. The infant regurgitated and became cyanotic, with shallow and irregular respirations. Many coarse râles were heard throughout the chest. During the day he had several bloody diarrheal stools and the abdomen became distended. Penicillin, 10,000 units, was started every three hours, but the infant was discovered dead with tremendous distention at 5:43 P.M.

Pathologic Report.—The abdomen contained 100 c.c. of cloudy, yellowish fluid. There was thick, purulent material over the bowel on the entire right side and in the pelvis, with adhesions of the bowel in this region. The arrangement of the organs was normal except that the appendix was plastered to the anterior rectal wall in the pelvis. Many loops of bowel showed small, hemorrhagic, and purulent areas on the serosa.

The jejunum appeared normal except for mild distention. The serosal surface of the lower ileum showed scattered areas of what appeared to be superficial abscesses surrounded by a hemorrhagic zone. In some areas these formed confluent masses measuring about 2.5 cm. in length. In the terminal ileum just at the ileocecal valve, the wall was thickened and hemorrhagic and in the mucosa there was a definite irregular, purulent ulcer. The appendix, as previously stated, was found in the pelvis, surrounded by purulent material. On removal from the body, the appendix was seen to be perforated in three different places. The tip of the appendix was gone, with the end open to the peritoneal cavity and the margin of the opening covered with purulent material. Two other perforations were apparently due to purulent

erosion in an inflamed appendix. The colon showed scattered serosal lesions in the ascending portion similar to those seen on the small bowel. In addition, there were seen numerous, scattered, small white nodules beneath the mucosa. There was no ulceration over these areas and they may represent abscesses in lymphoid follicles. The rectum was covered with purulent material and its mucosa was hemorrhagic and also appeared to be ulcerated. The mesentery was thick with lymph nodes.

Microscopic Report.—One section taken through the tip of the appendix showed almost complete necrosis. It was not possible to say whether there had been ulceration here, although some inflammatory exudate could be seen in the wall and serosal surface in parts of the section.

Another section showed three pieces of tissue taken through the appendix; the spaces between each piece represented the sites of perforation seen grossly. There were ulceration and marked necrosis with little inflammation of the wall, and the smallest piece of tissue seen here was made up of ulcerated wall with some exudate on all surfaces. Gram stains showed predominantly gram-negative rods with some gram-positive cocci and rods which appeared to be spore bearers.

Sections of the small intestine showed some inflammatory exudate on the serosal surface with necrosis. The wall of the intestine was involved in some places as deeply as the submucosa. Hemorrhage and necrosis were present at these sites. In a section taken through the ileum and ileocecal valve, there were ulceration and necrosis of the mucosa with some acute purulent exudate on the surface and in the wall.

A section through the terminal colon and rectum also showed ulceration of the mucosa with necrosis penetrating down into the muscularis. A good deal of necrosis was present surrounding and within the ulcerated sites.

One of the mesenteric nodes showed a central focal necrosis in which many bacteria could be seen. Few inflammatory cells were present, and the area was surrounded by many congested vessels.

DISCUSSION

It seems apparent from a study of these cases that a bizarre complication to the typical neonatal diarrhea has been encountered. In the two cases seen at this hospital *Bacillus coli* was found in the stool cultures. The role of this organism has been studied by McClure,[18] who concluded that the hemolytic colon and paracolon organisms were more prevalent in the stools of infants with diarrhea than of infants having normal stools. Numerous other organisms have at various times been ascribed an etiologic role in neonatal diarrhea. Hormaeche and associates,[13] in a large series of cases in Uruguay, found that 57 per cent of all enteritis in children under one year of age was due to the Salmonella or Shigella group of organisms. However, in 680 cases in which positive cultures were obtained, only 98 could fit the clinical picture which we encountered, and all of these occurred sporadically. Neter and Farrar[20] described twelve cases in which *Bacillus proteus* or *Bacillus morganii* or both were discovered in the stools; however, in no instance did agglutinins develop against the homologous micro-organisms. *Staphylococcus aureus hemolyticus* was found in the stools of three cases by Felson and Walorski.[11] They concluded that neonatal diarrhea was a local reaction to an extra-enteric infection. In support of this, Dick and associates,[9] have discussed an epidemic of diarrhea in children associated with mastoiditis. In 1941, Lyons and Folsom,[17] described three epidemics seen at the time of an influenza epidemic in the community. The infants involved were apparently helped by convalescent serum of patients having influenza. More recently, Buddingh and Dodd[4] have isolated a virus which

produced stomatitis and diarrhea in children. In the newborn infant diarrhea was the predominating feature. Light and Hodes[16] isolated a filterable virus from stools of infants with neonatal diarrhea which produced diarrhea in calves.

The clinical course of each of our infants was not unlike that seen in the uncomplicated cases of neonatal diarrhea. Loose, greenish white, foul smelling, watery stools, often passed with considerable force, was the presenting complaint in each instance. Dehydration and acidosis were constant findings. The only aspects of the course of these infants that differed from those in the typical cases were the marked abdominal distention leading to respiratory embarrassment seen in the terminal stages, and a rising temperature with little response to chemotherapy. Regurgitation with an increasing degree of acidosis was a common terminal finding. Rigidity and muscular spasm were not evident. The stools showed no appreciable change after perforation, and blood was found microscopically in only one case.

It is apparent that minor differences encountered were due to the perforation and subsequent peritonitis. To our knowledge only one other case of peritonitis associated with neonatal diarrhea has been reported and that was described by Kimberly.[14] In his series of six cases there was no ulceration and the pathogenesis of the peritonitis was unexplained. Abt,[1] has summarized the causes of fetal peritonitis, but he does not include ulceration accompanying diarrhea as a common cause. The etiologic factors which he stresses are: transmission of organism from the mother, syphillis, spontaneous rupture during fetal life, urinary tract malformations, gastrointestinal tract abnormalities, fetal appendicitis, bands and adhesions causing intestinal obstruction, and abnormalities of the biliary tract. Bullowa and Brennan,[5] in 1919, first reported perforation due to a meconium plug causing intestinal obstruction. Since that time there have been other reports[2] of peritonitis because of this mechanism. Peptic ulcers have been described in children and infants. Donovan and Santulli[10] reported a series of ten cases of peptic ulcer in children, but the youngest was in a 4-month-old infant and perforation did not occur in any of the cases. Bird, Limper, and Mayer,[3] in a review of the literature, summarized 245 cases of peptic ulcer in infants and children. Thirty-eight of these cases were in the newborn infant (1 to 14 days) with twenty-six duodenal and two gastric ulcerations. Eighteen of these perforated. Morrison[19] has reported an interesting type of ulceration in older children with malignant hypertension and uremia, but this has not been described in the newborn infant.

There seems to be little to offer these infants so far as therapy is concerned. A general regime aimed at combating dehydration, acidosis, and anemia is surely in order. Preventive measures are paramount in view of the absence of specific forms of therapy. Lembcke and associates[15] concluded that breast-fed babies were less prone to have neonatal diarrhea than those babies artificially fed. Their conclusions were based on two epidemics studied in Rochester, N. Y. Souther[21] has emphasized the importance of isolation precautions and Carson[6] has summarized the recent ideas concerning therapy in diarrhea of infants.

The latter stresses the importance of maintaining the normal fluid and electrolytic balance and of replacing the glycogen depleted from the tissues. Specific antibiotics are certainly indicated when the organism can be identified. Surgical intervention is undoubtedly futile in view of the multiplicity of lesions. However, Agerty and co-workers[2] have reported recovery of a case of peritonitis probably due to a meconium plug following surgical intervention. The general condition of the infant when such a complication ensues also often mediates against any operative procedures.

Gross inspection of the bowel in these cases revealed a similar picture. In two of the three cases the ulcerations were multiple. In all of the cases the small bowel was involved; however, in the last case described, the appendix seemed to be the primary source of pathologic lesions. The ulcers were not typical in their microscopic appearance. Hyperemia and infiltration with polymorphonuclear cells and central necrosis would indicate an acute process. More widespread loss of mucosa than of the underlying layers was evident, so that it would seem that the etiologic agent gained access from the lumen of the bowel. The pathologic picture seen here was unlike that described by other investigators only because of the presence of ulceration. Golvin and Emory[7] described superficial erosion of the mucosa of the jejunum and ileum with surrounding hyperemia. The typical findings of edema and hyperemia of the bowel wall with mild leucocytic infiltration have been described by Kimberly[14] and Greenberg and Wronker.[12] The microscopic picture observed in our cases did little to define the etiologic agent, and the exact pathogenesis of the ulceration, therefore, is undetermined.

SUMMARY

1. Three cases of nonspecific ulceration of the small bowel with peritonitis complicating neonatal diarrhea have been reported.

2. The clinical picture when such a complication occurs is characterized by abdominal distention, rising temperature, regurgitation, and an increase in the degree of acidosis.

3. The known therapy did not appreciably alter the course of the disease in these cases.

4. The etiology of neonatal diarrhea has been discussed.

5. The pathologic picture in these cases was that of multiple ulceration of the small bowel with perforation and peritonitis.

6. Causes of ulceration and peritonitis in the newborn infant have been briefly reviewed.

I should like to thank Dr. Francis F. Schwentker, Dr. Edgar B. Friedenwald, and Dr. Frederick B. Smith for their many helpful suggestions in preparing this paper. In addition, I should like to thank Dr. Schwentker for his kind permission to include the case seen at the Harriet Lane Home of the Johns Hopkins Hospital.

REFERENCES

1. Abt, I. A.: Med. Clin. North America 15: 611, 1931.
2. Agerty, H. A., Ziserman, A. J., and Shollenberger, C. L.: J. Pediat. 22: 233, 1943.
3. Bird, C. E., Limper, M. A., Mayer, J. M.: Ann. Surg. 114: 526, 1941.

4. Buddingh, G. J., and Dodd, K.: J. PEDIAT. **25**: 105, 1944.
5. Bullowa, J., and Brennan, R.: J. A. M. A. **73**: 1882, 1919.
6. Carson, M. J., and Carol, N.: Med. Jour. **6**: 323, 1945.
7. Colvin, S. H., and Emory M.: New Orleans Med. and Surg. J. **94**: 73, 1941.
8. Crowley, C. N., Downie, A. W., Fulton, E., and Wilson, G. S.: Lancet **2**: 590, 1941.
9. Dick, G. F., and Dick, G. H.: Am. J. Dis. Child. **35**: 955, 1928.
10. Donovan, E. J., Santulli, T. V.: Am. J. Dis. Child. **69**: 176, 1945.
11. Felson, J., and Wolarski, W.: Arch. Pediat. **59**: 495, 1942.
12. Greenberg, M., and Wronker, B. S.: J. A. M. A. **110**: 563, 1938.
13. Hormaeche, E., Surraco, N. L., Peluffo, C. A., and Aleppo, P. L.: Am. J. Dis. Child. **66**: 539, 1943.
14. Kimberly, A. M.: New Eng. J. Med. **220**: 664, 1939.
15. Lembeke, P. A., Quinlivan, J. J., and Orchard, N. G.: Am. J. Pub. Health **33**: 1263, 1943.
16. Light, J. S., Hodges, H. L.: Am. J. Pub. Health **33**: 1451, 1943.
17. Lyons, G. M., and Folsom, T. G.: Am. J. Dis. Child. **61**: 427, 1941.
18. McClure, W. B.: J. PEDIAT. **22**: 60, 1943.
19. Morrison, J. E.: Arch. Dis. Child. **20**: 90, 1945.
20. Neter, E. R., & Farrar, R. H.: Am. J. Digest. Dis. **10**: 344, 1943.
21. Souther, S. P.: Ohio State M. J. **39**: 30, 1943.

Case Reports

ARACHNODACTYLIA

THOMAS O. DORRANCE, M.D.
BLUFFTON, IND.

ARACHNODACTYLIA, or Marfan's syndrome, is characterized by a congenital symmetric malformation of the extremities consisting of considerable elongation and attenuation of the bones, more pronounced in the distal parts. This tendency to "spider hands and feet" is associated with muscular atrophy, and often with ocular and cardiac anomalies.

Andrew Rados, in March, 1942, in an excellent paper, reviewed all the 204 reported cases. Since his publication I have been able to find an additional forty-three cases in the literature, making a total of 247 reported cases up to June, 1946.

REPORT OF CASE

The patient, aged 6 years, was first seen in August, 1946. His symptoms were primarily muscle weakness and fatigue. The height was 52 inches (130 cm.), weight 46 pounds (2.09 kg.) and span 54½ inches (136 cm.). He was obviously tall and slender for his age. The musculature was weak, as evidenced by a stooped posture and forward drooping of the head. No subcutaneous fat was apparent. The eyes were extremely myopic, corrected with lenses to 20/25 vision bilaterally. The irides were tremulous, thin, and devoid of pigment. The lenses were tremulous but otherwise normal and the fundi appeared to be normal. The tonsils were enormously enlarged and there was an adenoid facies. The extremities, especially the hands and feet, were markedly elongated, and slender (Fig. 1) Physical examination was otherwise negative. Blood pressure was 106/80, pulse 90; there was no abnormality of the heart. Reflexes were present and normal.

The laboratory findings were as follows: Urinalysis negative; hemoglobin, 11.4 Gm. (73 per cent); R.B.C. 3,800,000; white count and differential normal; mazzini negative. The blood sugar was 124 mg. per cent.

Roentgenograms of the hands and feet showed pronounced elongation of the digits, (Fig. 2). Those of the urinary tract, chest, and skull were negative.

The past history of this case was not remarkable. He was delivered normally at term, weighing 8¼ pounds at birth. Development was normal with the eruption of the first tooth at 8 months, walking at 9 months and talking at 18 months. He started school at the age of 5 years and when last seen in June, 1947, he had successfully completed the first grade.

The family history was uninformative. There were no siblings. The parents and all the grandparents were normal individuals.

When seen in June, 1947, ten months after the original examination the patient had grown 2½ inches in height. The span measured 57 inches (142 cm.) as compared with 54½ inches (136 cm.) ten months before. He had gained 9 pounds. The tonsils and adenoids had been removed Aug. 20, 1946. The eyes and laboratory findings were the same as on the original observation. The child now wore a 6½ AAAA shoe, the foot measuring 9 inches in length and 2 inches in its widest dimensions, the hand 7 by 2¾ inches.

From the Caylor-Nickel Clinic, Bluffton, Ind.

DISCUSSION

This syndrome was first described in 1896 by Marfan. There are various theories as to the etiology, none of which are proved or accepted. The most tenable is that the condition results from a fault in the mesodermal cells of the embryo. About one third of the reported cases are hereditary and familial, the affection being transmitted by either sex through two or three generations, with about 50 per cent of the offspring affected. Marfan considered the deformities as possibly a result of trophic alterations of neuropathic origin but also mentioned the possibility of an endocrine pathogenesis similar to that of acromegaly.

Fig. 1.—Elongation of the hands and feet in a boy aged 6 years with arachnodactylia.

Clinically the syndrome of arachnodactyly seems to be closely allied to amyotonia congenita. There is marked atrophy of the entire musculature, especially in the extremities. Laxity of the ligaments and a resulting abnormal motility of the joints is a usual feature of the condition. The subcutaneous fat is diminished in amount. The bones of the hands and feet are relatively and absolutely increased in length, especially the metacarpals, metatarsals, and

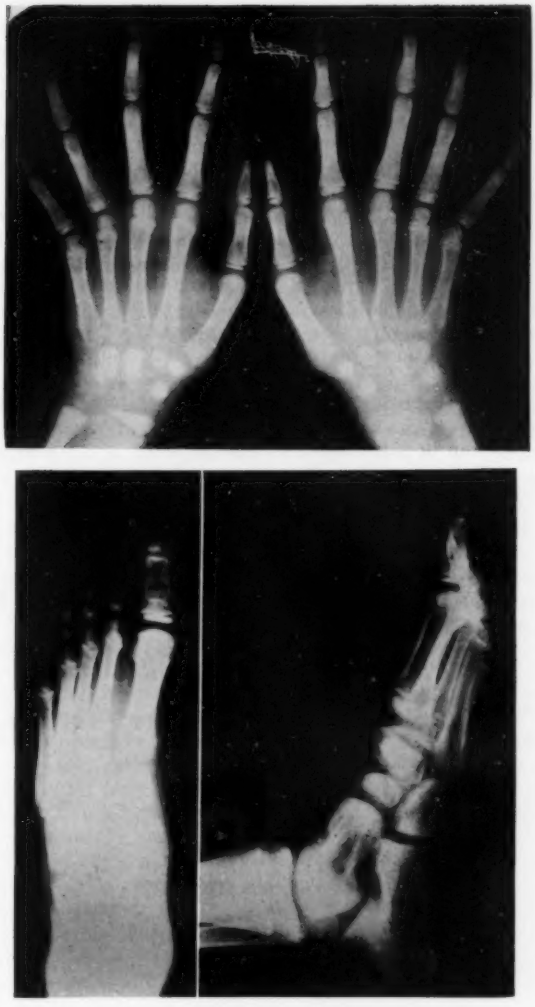

Fig. 2.—Roentgenograms showing marked elongation of the metacarpals, metatarsals, and phalanges.

phalanges. All the long bones of the body have a tendency to be increased in length. This lengthening becomes more pronounced toward the distal end of the limbs.

Abnormalities of the skull, usually toward dolichocephaly, are present in about 80 per cent of the cases. Prominent supraorbital ridges, frontal bosses, and prognathism are common. The palate is often narrow and highly arched.

Bilateral abnormalities of the eyes occur in over half the cases. Luxation or subluxation of the lens is the most frequent abnormality. Small pupils, tremulousness of the iris (irododonesis), strabismus, transient nystagmus, and a high degree of myopia are common. The fundus is usually normal.

Congenital heart disease has been noted in about a third of the cases. Perforate ventricular septum, patent ductus arteriosus, patent foramen ovale, and patent interauricular septum are among the lesions described.

Bodily proportions of the arachnodactylic child closely simulate pituitary gigantism as seen before puberty. The span is greater than the height, along with an increased height for the age. In pituitary gigantism, however, the bone age is usually retarded while in the former the bone age is increased by at least two years. Affected children are usually taller but weigh less than normal children of the same age. As a rule the mentality is excellent.

There is no satisfactory treatment. These individuals should lead a moderate sheltered life with a ban on strenuous physical exertion. There is a low resistance to respiratory infections and as a result few children with this disorder reach maturity. The majority have died of pneumonia.

The diagnosis can be established in the majority of cases by a casual survey of the patient as he enters the office, provided the physician is aware of the essential features of this syndrome.

CONCLUSIONS

A case of arachnodactylia in a 6-year-old male child is presented. The prominent features of this typical case were elongation of the feet and hands, muscular atrophy, and iridodonesis.

REFERENCES

1. Rados, A.: Arch. Opth. **27**: 477, 1942.
2. Baer, R. W.: Brennemann's Practice of Pediatrics IV: 26, Hagerstown, Md., 1938, W. F. Prior Co.
3. Young, M. L.: Arch. Dis. Child. **4**: 190, 1929.
4. Schneider, W. F.: J. PEDIAT. **27**: 583, 1945.
5. Dvorak-Theobald, G.: Am. J. Opth. **24**: 1132, 1941.
6. Gray, H.: Arch. Int. Med. **75**: 215, 1945.
7. Olcott, C. T.: Am. J. Dis. Child. **60**: 660, 1940.
8. Ellis, R. W.: Arch. Dis. Child. **15**: 267, 1940.

CONGENITAL HEMOLYTIC ANEMIA OF THE NEWBORN INFANT CAUSED BY ISOIMMUNIZATION WITH AGGLUTINOGEN B

ABRAHAM NATHAN, M.D., FREDERICK C. GREEN, M.D., AND GEORGE WEISS, M.D.
NEW YORK, N. Y.

IN 1940 Landsteiner and Weiner[1] discovered the Rh antigen. In 1941 Levine and co-workers[2] demonstrated the relationship between Rh incompatibility and erythroblastosis fetalis. Since then, the fields of hematology and pediatrics have been enriched by the voluminous work done in exploring the Rh subgroups and their roles as causative agents of hemolytic anemia of the newborn infant. However, not all cases of erythroblastosis are caused by the Rh antigen-antibody reaction. The A or B agglutinogens, commonly present in many individuals, can, on occasion, cause hemolytic anemia of the newborn with jaundice.

As early as 1905, Dienst[3] suggested that heterospecific pregnancies may give rise to morbid conditions in mother and infant. McQuarrie[3] furthered this theory by showing that toxemias of pregnancy and subsequent infant morbidity increased when an incompatibility existed between the mother's and infant's bloods. Ottenberg[3] and La Vake[4] proposed that a leakage of fetal blood during pregnancy resulted in isoimmunization. Hirzfeld[3] stated succinctly that the fetus could be damaged in heterospecific pregnancies due to the passage of maternal antibodies into the baby's circulatory system.

Johsson[5] and others[6-8, 13] proved that the titer of anti-A or anti-B agglutinins rises during heterospecific pregnancies. Titers of 1:58 anti-A agglutinins were observed in Group O nulliparous women, whereas those Group O women who gave birth to Group A children showed an anti-A titer of 1:215.[7] The literature has no comparable studies for Group O mothers with Group B children. Why the antigens A or B are not responsible for more cases of congenital hemolytic anemia is explained in several ways. The most widely held view maintains that 80 per cent of the population are "secretors" (contain the specific group substances in their tissues and secretions, e.g., saliva) whereas 20 per cent of the population are "nonsecretors."[9] This condition enables the "secretors" to protect themselves from the hemolytic effects of isoimmunization.[9-12] Tovey[14] gives four reasons why the fetus enjoys protection from the mother's agglutinins in heterospecific pregnancies: (1) lack of placental permeability to anti-A or anti-B agglutinins; (2) fetal plasma neutralizes the A or B antibodies; (3) fetal erythrocytes are not sufficiently sensitive; and (4) the A and B antibodies do not react very well at body temperature. Weiner,[11] too, supposes a placental barrier for the anti-A or anti-B isoagglutinins because of their relatively large molecular size.

There are cases on record proving the presence of a hemolytic anemia of the newborn infant resulting from the isoimmunization by the agglutinogen A or its subtype A_1.[7, 9, 15, 16]

The literature concerning Group B isoimmunization is very sparse. In a review of 100 cases of erythroblastosis, Boorman and associates[16] found two cases where the anti-B titer was significantly high to suspect the B agglutinogen as the cause of the anemia. La Vake[4] quotes Koucky who delivered a Group O, Rh-positive mother of a Group B Rh-positive baby. The infant became severely jaundiced and anemic. The anti-B titer five weeks post-partum was 1:1,600.

From the service of Dr. Morris Gleich, Director of Pediatrics, Harlem Hospital, New York.

Eight months later the tier had fallen to 1:500. The most recent report published by Gruber and associates,[17] which, although a bona fide case of Group B isoimmunization, is not the first case to be so reported in the light of the foregoing discussion.

We wish to report another case of Group B isoimmunization.

On Feb. 12, 1947, M. C., a 6 lb. 15 oz. Negro male child was delivered spontaneously at Harlem Hospital. The mother was gravida ii, para ii. The first pregnancy terminated spontaneously at term. The mother never had any transfusions and her blood Kahn reaction was negative.

The baby at birth presented no clinical abnormalities. However, an icteric tinge was noted on the second day of life. The jaundice began to deepen quickly, so that by the third day the baby's skin and mucous membranes were obviously yellow. The physical examination at this time was essentially negative except for a barely palpable liver. The spleen was not palpable. No dehydration was present. The blood findings on the third day showed a moderately severe anemia but the infant did not appear critically ill (Table I).

TABLE I

DAY OF LIFE	% HEMOGLOBIN (SAHLI)	ERYTHROCYTES (MILLIONS)	% HEMATOCRIT	NUCLEATED ERYTHROCYTES PER 100 LEUCOCYTES
3	68	2.3	35	3
4	58	4.2	20	15
6	56	3.3	28	12
11	75	3.9	36	4

The mother was typed as Group O Rh-positive and the baby was found to be Group B Rh-positive. The following day (fourth) the liver was palpable 1.5 cm. below the costal margin. The hemoglobin and the red cell count showed a precipitous fall (Table I). An immediate transfusion of 50 c.c. Group B Rh-positive blood was given intratibially. Other blood findings were:

Icteric index		100
Leucocytes		9,800
Diff.:	Myelocytes	1%
	Premyelocytes	4%
	Metamyelocytes	3%
	"Stabs"	3%
	Polynuclears	68%
	Monocytes	5%
	Lymphocytes	16%

The smear showed marked poikilocytosis and anisocytosis.

Recovery took place at a satisfactory rate. The jaundice diminished while the hemoglobin and erythrocyte counts increased. On the sixth day the liver was no longer palpable. On the eleventh day the mother took the baby home. The hemogram (Table I) on discharge still gave evidence of a moderate anemia, but the general condition of the infant was such that we permitted the discharge. During the entire course of his illness, the baby was afebrile and had normal yellow stools. The baby's blood Kahn was negative.

We requested Dr. N. Rosenthal to make a more complete blood study to determine, if possible, the causes of the hemolytic anemia. The following results were obtained (Table II).

No atypical agglutinins were found. However, the mother had an anti-B agglutinin titer of 1:2,048.

About one month later the mother and child returned for a check-up. The baby's growth and development were normal and the baby was in excellent health. The anti-B agglutinin titer of the mother's blood was repeated and found to be 1:256.

The father and other sibling were not available for blood studies.

TABLE II

MOTHER	BABY
Group O	Group B
Rh+	Rh+
Rh′ negative	Rh′ negative
Rh″ negative	Rh″ negative
Hr+	Hr+

COMMENT

This is evidently a case of congenital hemolytic anemia which occurred as a result of a heterospecific pregnancy. The baby was not examined to determine whether he was a "secretor" or "nonsecretor." However, we see that the patient's blood was susceptible to the high titer of his mother's agglutinins and subjected to considerable destruction.

A point has been made that it would be wiser to give Group O blood for transfusions in these cases.[17] Group O erythrocytes are not subject to the hemolytic actions of the anti-B agglutinins, and therefore they will more readily preserve the patient's blood level. The patient's recovery will thus be hastened and maintained. We tranfused our case with Group B blood before the true nature of the underlying condition was realized. The results achieved, nevertheless, were good.

SUMMARY

A case of isoimmunization by the agglutinogen B as a result of a heterospecific pregnancy has been discussed in detail. A suggestion that Group O blood be given in similar cases is noted and advised. Included is a complete review of the literature.

We wish to thank Dr. Nathan Rosenthal, Attending Hematologist at Harlem Hospital, for his valuable assistance in the blood studies.

REFERENCES

1. Landsteiner, K., and Weiner, A. S.: Studies on an Agglutinogen (Rh) In Human Blood Reacting With Anti-Rhesus Sera and With Human Isoantibodies, J. Exper. Med. **74**: 309, 1941.
2. Levine, P., Katzin, E. M., and Burnham, L.: Isoimmunization in Pregnancy, J. A. M. A. **116**: 825, 1941.
3. Cited from A. S. Weiner: Blood Groups and Transfusions, ed. 3, Springfield, 1943, C. C. Thomas, Chap. XX, p. 328.
4 La Vake, R. T.: Causes of Toxemia of Pregnancy, Lancet **63**: 51, 1943.
5. Johsson, B.: Zur Frage Der Heterospezifischen Schwangerschaft, Acta. Path. Micro. Scand. **13**: 424, 1943.
6. Smith, G. H.: Iso-agglutinin Titers in Heterospecific Pregnancy, J. Path. Bact. **57**: 113, 1945.
7. Polayes S. H., and Ohlbaum, C.: Erythroblastosis Fetalis Unrelated to Rh Factor, Am. J. Clin. Path. **15**: 467, 1945.
8. Boorman, K. E., Dodd, B. E., and Mollison, P. L.: Isoimmunization to Blood Group Factors A, B, Rh, J. Path. Bact. **57**: 157, 1945.
9. Polayes, S.: Erythroblastosis in Rh+ Mothers, Am. J. Dis. Child. **69**: 99, 1945.
10. Halbrecht, I.: Role of Hemoagglutinins Anti-A and Anti-B in Pathogenesis of Jaundice of Newborn, Am. J. Dis. Child. **69**: 428, 1944.

11. Weiner, A. S.: Pathogenesis of Congenital Hemolytic Disease, Am. J. Dis. Child. **7**: 14, 1946.
12. Hallwright, W. W.: Hemolytic Disease of Newborn, New Zealand M. J. **45**: 2, 1946.
13. Weiner, A., Oremland, B., Hyman, M., and Samwick, A.: Transfusion Reactions, Am. J. Clin. Path. **11**: 116, 1941.
14. Tovey, G. H.: A Study of the Protective Factors in Heterospecific Blood Group Pregnancy and Their Role in the Prevention of Hemolytic Disease of Newborn, J. Path. Bact. **57**: 295, 1945.
15. Austin, A. B.: Heterospecific Pregnancy as a Positive Cause of Erythroblastosis Fetalis, Brit. M. J. **2**: 123, 1946.
16. Boorman, K. E., Dodd, B. E., and Mollison, P. L.: Incidence of Hemolytic Disease of Fetus in Different Families, J. Obstet. Gynec. Brit. Emp. **51**: 1, 1944.
17. Gruber, S., Litvak, A., and Jacobi, M.: A Case of Erythroblastosis Fetalis Caused by Isoimmunization With Agglutinogen B, J. Pediat. **29**: 518, 1946.

CARBAMINOYLCHOLINE (DORYL) IN THE TREATMENT OF CONGENITAL MEGACOLON

JACOB GREENBLATT, M.D.
STAMFORD, CONN.

THE therapeutics of congenital megacolon up to the age of 4 years is medical rather than surgical. Such procedures as sympathectomy and colectomy[1-3] are often too dangerous in infancy, and are not completely without danger or so certain of good results that even in older age groups conservative measures should be tried first. In surgically treated patients, drug therapy provides a valuable adjuvant[1] whenever relief is incomplete. Medical management, however, leaves much to be desired, as is evident by the large number and variety of drugs recommended, and from the fact that many cases eventually require surgery. Hence, any promising addition to our medical armamentarium is welcomed in the hope that it may prove superior to any heretofore known drug.

A review of the literature reveals that among the drugs used in megacolon are the choline derivatives (mecholyl bromide, urecholine),[4-6] neostigmine, syntropan,[7] atropine,[8] spinal anesthesia[9] (which is also used as a test to determine the suitability of the bowel for sympathectomy),[10] depropanex,[11] and parathormone.[12] There is no report on the use of carbaminoylcholine in congenital megacolon, except for one by van Gelderen.[13] He employed it hypodermically to determine the advisability of sympathectomy but did not treat his patients with it. This article came to our attention as an abstract in the *Journal of the American Medical Association* (**132**: 416, 1946) one month after our experiment was begun.

The use of parasympathicomimetic compounds finds its rationale in the theory that Hirschsprung's diseases is a result of a type of imbalance of the sympathetic and parasympathetic nervous systems in which the latter requires stimulation. There are other ideas as to the cause, but they have been adequately discussed elsewhere.[1, 8] Varying amounts of success have attended the use of the compounds enumerated above. Until they were available, there was much less in the way of good results from medical treatment consisting of repeated enemas, liquid petrolatum, laxatives, and anal dilatation. However, the use of frequent enemas (every three days) while there are no bowel movements is not to be belittled in any regime for megacolon therapy. This prevents overdistention and subsequent loss of tone of the large bowel, until such time that the drug or sympathectomy becomes effective. This and supportive treatment with vitamins and adequate diet are important in the care of megacolon. These adjuncts were used throughout the management of the case to be presented, until carbaminoylcholine took effect.

Carbaminoylcholine[14] (carbaminoylcholine chloride, Doryl, Lentin) is a parasympathicomimetic drug distinguished from other choline derivatives by its more powerful action on the urinary bladder and gastrointestinal tract. Its latter characteristic would suggest its use in megacolon. This compound is the most potent and most toxic of the choline series, but the margin of safety is practically that of acetyl B methyl choline. Its action appears more slowly and lasts longer than that of any other choline compound, and atropine is less effective in overcoming the effects of doryl. This drug has the advantage of

being stable in body fluids, and can be taken orally in doses of 0.2 to 2.0 mg. b.i.d. Various amounts can be tolerated. It is used in such conditions as urinary retention, peripheral vascular disease,[15] increased ocular tension, and myasthenia gravis.

Single case reports do not establish the value of a drug, but they do serve to stimulate studies on larger groups. The rarity of congenital megacolon (varying from 1:9,000 to 1:30,000 hospital admissions[3] alone justifies the presentation of single case studies. Furthermore, the value of this report is enhanced by three sets of control periods; namely, one without any medication, one under medication with several of the recommended drugs, and one during the administration of carbaminoylcholine. These considerations, in addition to the all-important fact that medical treatment is a necessity during infancy, warrant the presentation of a single case, in which treatment with doryl has been more successful than with any other medicament.

R. K., a white male child, was born Nov. 12, 1944. Delivery was normal and the newborn period was uneventful except for a mild attack of diarrhea that responded to modification of formula. Family history is noncontributory; he has a normal sister born in 1941. He weighed 8 lbs., 8 oz. at birth, and was placed on an evaporated milk formula. Nothing unusual was noted about his bowel movements, until he was one month of age, when he had not moved his bowels for five days. From then on he was always constipated. Examinations did not reveal any anal or rectal obstruction. He became increasingly distended despite the use of prune juice, magnesia magma, and increase of sugar in the formula. Enemas were often necessary.

At the age of 3 months, the protuberance of his abdomen was quite marked. At the level of the umbilicus the abdominal circumference was 17 inches; while the circumference of the chest was 15¾ inches. A barium enema on the next day revealed a dolichocolon. He was started on 5.5 mg. syntropan three times a day; this was increased to a dose of 13 mg. five times daily, to no avail. Mineral oil was also given, but enemas were necessary to prevent overdistention. On April 9 when he was 5 months old, neostigmine, in the form of prostigmine bromide, was given orally in the dose of 2 mg., but emesis and severe cramps resulted.

He was then hospitalized at the Babies Hospital, New York, where x-rays revealed a marked dilatation of the entire colon, sparing only the rectum and lower sigmoid. This type of megacolon has the poorest prognosis according to Grimson.[16] In that institution he was treated with urecholine (beta methyl choline urethane),[17] which is a choline derivative having a selective action on the urinary and gastrointestinal systems with fewer side effects than doryl. Two weeks of this therapy resulted in daily bowel movements, but anorexia and emesis developed. Therapy was discontinued, and daily movements continued for the following two to three weeks, only to be followed by severe constipation. On June 13, 1945 (age, 7 months), he was given mecholyl bromide in gradually increasing doses up to 100 mg. twice a day orally for one month without improvement. Instead, he lost weight and developed an anemia (hemoglobin red blood cells 3,400,000) which responded to a transfusion, liver, iron, and vitamins. No further specific therapy was given and efforts were concentrated on improving the poor nutrition. For the next month he would have a bowel movement about every three days, but required enemas to reduce distention. On September 8 (age, 10 months) therapy with urecholine was again resumed. Again his hemoglobin began to drop (64 per cent), and by November 1, it was apparent that there was no response to this drug, in so far as bowel movements were not regular.

His abdomen remained distended when syntropan was tried again on November 13 (age, 1 year) in doses of 15 mg. daily. This was increased to 60 mg. in divided doses daily for one and one-half weeks without definite benefit. It was discontinued on December 10, by which time the circumference of his abdomen had increased from 18½ inches to 20½ inches in one month. His bowels were emptied with repeated enemas, and then for a period of two and one-half months he had spontaneous daily bowel movements. However, when he was seen on March 19, 1946, he had had no bowel movements for one week, and his abdomen was becoming distended. Prostigmine bromide was then tried in doses of 2.5 mg. three times a day. There were daily bowel movements for one week, and then this dose had to be given five times daily to produce regular movements. This improvement caused his mother to give the medication irregularly, and at one point (age, 1 year 7 months) she suddenly increased the dose to 2.5 mg. six times daily with emesis and cramps resulting. This was relieved by an injection of atropine gr. 1/500. His bowel movements again became infrequent, and then the dose of neostigmine was gradually increased to 2.5 mg. six times daily but despite the use of this large dose, by July 2 (age, 1 year 8 months) the bowel movements had again become very infrequent.

It was then decided to follow Peterman's[6] treatment schedule using mecholyl bromide 0.05-0.2 Gm. once or twice daily, daily enemas, and mineral oil. In this case the dose of mecholyl was gradually increased to 250 mg. before noon and 200 mg. afternoon, but by August 20, after seven weeks of trial with mecholyl, there was no improvement. In order to potentiate the effects of this drug, it was decided to take advantage of the cholinesterase-inhibiting action of neostigmine, and the latter was added to mecholyl. Neostigmine was given in doses of 5 mg. in the morning and 2.5 mg. in the afternoon; mecholyl bromide was given in doses of 200 mg. twice a day. All this was to no avail, and after two and one-half weeks on this therapy, his abdomen remained distended and enemas were necessary.

The repeated failure of the most promising and well-recognized medications in the treatment of this patient prompted a search for a drug heretofore untried in congenital megacolon. Carbaminoylcholine seemed a likely possibility, particularly because of its selective action on the intestines.

Accordingly on Sept. 6, 1946 (age 1 year, 10 months), doryl (carbaminoylcholine chloride Merck) was begun in doses of ⅓ mg. three times daily, after meals, orally. There were no toxic effects, and he had occasional bowel movements. The dose was carefully increased to ¾ mg. after meals three times daily and by October 3 he was having one bowel movement daily. At the end of that month it was decided to discontinue medication, both in order to have a control period, and to determine whether the stimulus given by doryl would establish daily movements. He had regular bowel movements for one and one-half months thereafter. However, by Jan. 13, 1947, his abdomen was again becoming distended (circumference 21½ inches), and he did not have bowel movements for three to four days at a time, and then only following enemas. Doryl was again resumed in doses of ¾ mg. after meals three times a day, but he still required enemas for the next nine-day period, and his abdomen increased to 21¾ inches in circumference. Not until doryl was increased to 1 mg. after meals three times a day did he begin to have daily bowel movements starting on February 1 (age, 2 years, 2 months). The only episode of toxicity occurred when he was once given ¾ mg. five times daily and emesis developed for one day. He received 1 mg. three times daily and mineral oil daily until April 24, at which time it was reduced to 1 mg. twice daily with daily bowel movements continuing. This period of eight and one-half months (at the time

of writing) of regular bowel movements while taking doryl (except for a one and one-half month control period) stands in sharp contrast to the results of any other medication in this case of congenital megacolon.

I would like to express my appreciation to Miss Carlson, librarian of the American Cyanamid Co., for her assistance.

REFERENCES

1. Herman, L. G.: Surg. Clin. N. A. 1170, 1946.
2. Penick, R. M.: J. A. M. A. **128:** 423, 1945.
3. DeTakats, G., and Biggs, A. D.: J. PEDIAT. **13:** 819, 1938.
4. Law, J. L.: J. A. M. A. **114:** 2537, 1940.
5. Law, J. L.: Am. J. Dis. Child. **60:** 269, 1940.
6. Peterman, M. G.: J. PEDIAT. **27:** 484, 1945.
7. DeSanctis, A. S., and Larkin, V. DeP.: N. Y. State J. Med. **45:** 310, 1945.
8. Klingman, W. O.: J. PEDIAT. **13:** 805, 1938.
9. Stebbins, S. I.: Am. J. Surg. **27:** 107, 1935.
10. Morton, J. J., and Scott, W. J. M.: Ann. Surg. **92:** 919, 1930.
11. Reeves, R. J. and Harrison, E. K.: Radiol. **28:** 731, 1937.
12. Sheldon, L., Kern, R. A., and Hakansson, E. G.: Am. J. Med. Sc. **184:** 94, 1932.
13. Van Gelderen, C.: Acta chir. Scandinav. **94:** 81, 1946.
14. Goodman, L., and Gildman, A.: Pharmacological Basis of Therapeutics, New York, 1941, The Macmillan Co.
15. Starr, I.: Am. J. M. Sc. **193:** 393, 1937.
16. Grimson, K. S., Vandegrift, H. N., and Dratz, H. M.: Am. J. Dis. Child. **68:** 102, 1944.
17. Starr, I., and Ferguson, L. K.: Am. J. Med. Sc. **200:** 372, 1940.

ECTROMELIA AND ASSOCIATED DEVELOPMENT DEFECTS

HAROLD E. STADLER
INDIANAPOLIS, IND.

CLOSE collaboration between biochemist and embryologist has led to a greater understanding of the origin of the so-called "congenital anomalies." Experimental production in animals of some of the developmental defects observed in man has been invaluable in this broad study though it is true that many factors employed experimentally (electrical and traumatic stimulation, temperature change, and various dietary deficiencies) do not operate in carefully studied human subjects.

This report concerns itself with observations made of an infant who at birth was found to be afflicted with multiple deformities and absence of one upper extremity.

A. T. was born on Jan. 18, 1946, and his birth weight was 7 pounds. The mother was a 21-year-old unmarried Negro girl. The health of the father was excellent and congenital deformities in each family were unknown. A Wassermann test performed on the mother was negative. The mother stated that during her pregnancy she gained 20 lb. (from 120 to 140 lb.) Quickening occurred at 16 weeks and no abnormality of fetal movement was experienced. She denied edema of the legs, and the abdomen did not enlarge excessively. No infection occurred during her pregnancy and she was questioned particularly about viral infections.

The infant nursed poorly with frequent nasal regurgitation, and fever to 102° F. occurred on the fifth day after birth, with a rise to 104° F. on the eighth day. He was transferred to the pediatric service where the following abnormalities were noted:

The left upper extremity was absent, the stump at the shoulder being well healed. The right upper extremity appeared small, due to contracture of the elbow and absence of the thumb and index finger. The hand presented a smooth, narrow appearance. The left lower extremity was slightly longer than the right lower extremity (one centimeter) and had a *genu recurvatum* deformity. The hips were normal.

Prominence of the forehead suggested hydrocephalus, but the occipitofrontal circumference was 36 cm. The scleroties were markedly bluish and bilateral atresia of the external auditory canals was present with thickening of the lobes of the ears. Hypoplasia of the mandible was evident with limited motion of the temporomandibular joints. The hard palate was narrow and high and ended posteriorly at a narrow slit which represented the throat. There was a generalized fine papular rash, most marked on the face.

Laboratory: There was no abnormality of the urine. The hemoglobin was 14 Gm. per 100 c.c. of blood, the leucocyte count, 10,250 with 45 neutrophiles, 2 bands, 1 eosinophile, and 52 lymphocytes.

Radiologic Study: The left upper extremity was absent with exception of a rudimentary humerus 19 mm. in length and 2 to 3 mm. in width in comparison to the right humerus, which was 75 mm. in length and 5 to 12 mm. in width. A flexion contracture of the right elbow was seen with relative shortening of the radius in comparison to the ulna. No carpal ossification centers were seen and

From the Department of Pediatrics, Indianapolis City Hospital.

A.

B.

C.

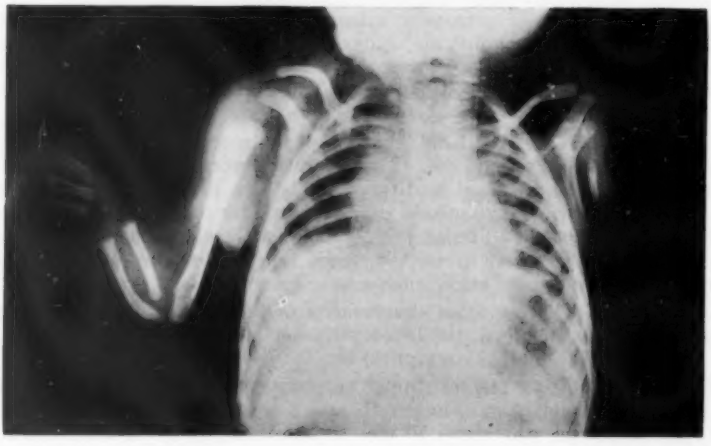

Fig. 1.—A. T. when 4 months of age, showing: *A*, Absence of left upper extremity and the genu recurvatum; *B*, Developmental abnormalities of the right upper extremity; *C*, Skeletal changes in the right upper extremity and the rudimentary humerus on the left.

there were only three digits, one of which included a metacarpal and two phalanges. The other two digits each consisted of a metacarpal and three phalanges.

The epiphyses at the left knee were unusually flat. There was an ossification center for the upper end of the tibia as well as the lower end of the femur. *Genu recurvatum* deformity was present on the left with posterior displacement of the femur in relationship to the tibia.

Course: Growth was slow with the weight on May 18, 1946 (age 4 months), found to be 8 lb., 10 oz., and head circumference 41 cm. in the occipitofrontal plane. The weight was 10½ lb. at 8 months of age. There was a constant nasal discharge.

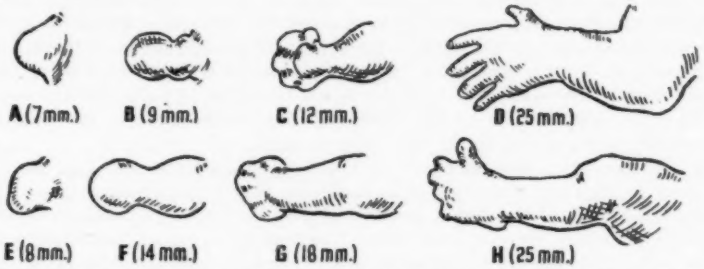

Fig. 2.—Stages in the development of the limbs between 5 and 8 weeks. (×6.) Upper row, upper limb; lower row, lower limb. (Arey: Developmental Anatomy, Philadelphia, 1940, W. B. Saunders, ed 4.)

DISCUSSION

The development of the extremities follows this pattern according to Arey.[1]

"The limb buds appear late in the fourth week as lateral swellings but due to early dominance of the head-neck region the arms seem to be located far down the body. The distal end of the limb bud flattens and a constriction divides this paddle-like portion from a more proximal, cylindrical segment. Later, a second constriction separates the rounded part into two further segments and the three divisions of arm, forearm, and hand or thigh, leg, and foot are then respectively marked off. Radial ridges, separated by grooves, first foretell the location of digits. These elongate into definite fingers or toes, and rapidly project beyond the original plates; the latter by a slower rate of growth becomes restricted to webs about the basal ends of the digits. The thumb separates widely from the index finger and the same is true of the great and second toes.

"The upper limb buds appear first, begin their differentiation sooner and are earlier in attaining their final relative size. Not until the second year of childhood does the leg equal the arm in length; its continued faster elongation throughout childhood is a conspicuous part of post-natal development."

Stockard[2] pointed out that embryonic growth is marked by a changing rate for the organism as a whole. The variation in rate of growth must remain within definite limits in order that a normal individual be produced. Various tissues have their specific rate of elaboration, which means that inequalities will be present with potentiality for an equalization by cessation of protoplasmic activity.

The tissues which had gained the most rapid growth would then (if growth ceased) be forced to start again on equal terms with other parts. Balance under these circumstances would indicate an inequality essential for normality. Type differences in malformation would depend upon the period of growth in which the disturbance appeared with the same general explanation applicable for

teratologic variations. Experimentally, the developmental rate (probably actually the oxidation rate) could be modified by temperature suppression.

Streeter[3] stressed "the normal disparity in the quality or vitality of different tissues of the body, inherent in the germ-plasm and hereditarily transmitted." Any tissue could evidence an abnormal variation in growth and a hypertrophic or atrophic extremity would strongly reflect the propensity of its anlage for growth. Absence of the primordium would indicate an extreme instance (agenesis). Streeter considered as intermediate in form such structural abnormalities as syndactyly and polydactyly.

Instances of intrauterine amputation would be considered at a level between defective development and true agenesis under this concept and limb bud tissue islands would indicate poor quality for growth. These tissue islands have been noted during the fourth fetal month as degenerated fibrous masses. The amputation stump would be formed by compensatory action of normal adjoining tissues. The so-called amniotic band (adherent hyalinized tissue) would have the same significance as the healed stump or the groove, re-establishment of the equilibrium of tissues by the time of birth.

It is to be noted that as early as 1890, Hirst and Piersol[4] had studied the problem of human monstrosities and concluded that cases of hemimelus (absence or maldevelopment of the distal portion of an extremity), phocomelus (shortening or rudimentary development of an extremity with an essentially normal hand or foot), ectromelus (absence of one or more extremities), and micromelus (morphogenetically normal but small extremity) are to be explained on a basis of arrested development, and this mechanism must be distinguished from intrauterine amputation by amniotic bands.

An interesting and correct case of intrauterine amputation was reported by Latta.[5] His specimens consisted of identical twins which had been still-born. One twin was entirely normal, the other showed absence of the left leg distal to the knee (hemimelus). The stump was covered with skin through which protruded a sharp broken end of fibula. The right ankle appeared to have been involved in a constrictive process with vascular changes distal to the constriction.

Latta justifiably stated that "should these defects have been of such nature as to be hereditarily transmissible, both individuals would have been defective because of their identical inheritance. Secondly, in this one deformed individual are seen, in addition to the amputated leg, what are interpreted as various stages in the process leading to the result."

A case similar to that reported here is the one of Bizzaro[6] who described total absence of the right upper and lower extremities and of the left fibula and fifth toe. At the right hip was a small pedunculated knob which had the appearance of a toe and which was the sole representative of the right lower limb. There was a valgus deformity of the left foot and full passive extension of the left knee was impossible. A radiogram of the shoulder presented a complex of an overdeveloped acromium with complete absence of the glenoid.

The extreme instance of agenesis involving the extremities is the amelus monster which has been reported by Killingsworth and Engledow[7] and by Levy.[8]

The diffuse developmental aberration in the case of A. T. reported here is demonstrated in the absence of one upper extremity and malformations of the other upper extremity. It is quite likely that the deformity of the left knee was not a part of the deficiency process. Chandler[9] has stated that *genu recurvatum* is a minor congenital anomaly when it occurs under such circumstances and is probably due to hyperextension of the knee *in utero*.

Reflecting also the diffuse nature of the disturbance in A. T. were malformations of the ears, jaw, and throat. Furrows were entirely absent on the

extremities and with regard to the right hand, it was clearly evident that the lack of two digits constituted a deficiency rather than an amputation process.

The general findings here are somewhat at variance with the criteria laid down by Cummins.[10] This author has offered the following division between the agenetic and amputation groups:

"1) Agenesis is limited to one extremity *commonly* while true amputations are multiple and typically occur in two or more extremities.

"2) The most extreme defect of agenesis is expressed in the skeleton. At the distal end of the affected member the soft tissues often build up a diminutive and imperfect construction of the suppressed part.

"3) There is a semblance to a surgical stump in intrauterine amputation and the identity as a true amputation is evidenced not only by the aspect of a repaired wound, sometimes with adherent fibrous tissue, but also by the occurrence of one or more furrows."

SUMMARY

There is presented an infant who showed diffuse developmental defects involving the upper extremities and head. It is not possible to establish definitely either a hereditary or infectional basis for the skeletal changes present.

Evidence that amniotic bands were responsible for "intrauterine amputation" in this case is entirely lacking.

The author expresses his appreciation to Dr. J. K. Berman for his valuable suggestions and to Joseph F. Goldsmith for his help with the photographic details.

REFERENCES

1. Arey, L. B.: Developmental Anatomy, Philadelphia, 1940, ed. 4, W. B. Saunders, pp. 159-160.
2. Stockard, Charles R.: Am. J. Anat. **28**: 115, 1920-21.
3. Streeter, George L.: Focal Deficiencies in Fetal Tissues and Their Relation to Intrauterine Amputation. Contributions of Embryology, 1930, Carnegie Institute of Washington, vol. 22, No. 126-133.
4. Hirst, B. C., and Piersol, G. A.: Human Monstrosities, Edinburgh and London, 1892, Young J. Pentland, Part I.
5. Latta, J. S.: Am. J. Obst. & Gynec. **10**: 640, 1925.
6. Bizzaro, A. H.: Lancet **1**: 898, 1936.
7. Killingsworth, W. Price, and Engledow, R.: Am. J. Dis. Child. **63**: 914, 1942.
8. Levy, J.: South. Med. J. **34**: 1085, 1941.
9. Chandler, F. A.: Orthopedics. Brennemann's Practice of Pediatrics, Hagerstown, Md., 1942, W. F. Prior Co., vol. 4, ch. 34, p. 22.
10. Cummins, Harold: Congenital Amputations. Brennemann's Practice of Pediatrics Hagerstown, Md., 1942, W. F. Prior Co., vol. 4, ch. 24, p. 1.

Clinical Conference

CONFERENCE AT DUKE HOSPITAL

AUG. 28, 1947

Clinic on Nephritis and Nephrosis

DR. R. M. WILHOIT.—M. J., an 8-year-old Negro girl, was brought to Duke Hospital Aug. 22, 1947, with a chief complaint of a poor appetite for five days, unaccompanied by nausea, vomiting or change in bowel habits. For the previous three months she had had sores on her lower legs which had become worse during the three weeks prior to admission. She had not had any upper respiratory infections. Two days prior to admission the patient had swelling of her face, mainly about her eyes, and, on the day of admission, swelling of her ankles. On entry, her temperature was 37.8° C. (100° F.), her pulse rate 68, her respiratory rate 20, and her blood pressure 160/120 bilaterally. Over her lower legs there were many crusted lesions, the majority measuring 1 to 2 cm. in diameter. On removal of the crusts, a small amount of pus could be expressed. There was some pitting edema of the ankles. Examination of the heart, lungs, and abdomen revealed no abnormality. The urine contained 2+ albumin, 15 to 25 red blood cells per high-power field, many white blood cells, and 1 to 2 granular casts. The hemoglobin was 8.5 Gm., R.B.C. 3,500,000 and W.B.C. 9,800 with an increase in neutrophiles. No sickling of the red blood cells occurred. Cultures of the lesions on the legs showed *Streptococcus hemolyticus* and *Staphylococcus aureus*. Blood cultures were negative. The blood nonprotein nitrogen was 108 mg. per cent, the total proteins 7 Gm., albumin 3.4 Gm., globulin 3.6 Gm., and an albumin-globulin ratio of 0.94.

On admission, 10 c.c. sterile 25 per cent magnesium sulfate were injected intramuscularly and repeated in two hours. The patient was placed on complete bed rest, with a salt-free, low protein diet, and 10,000 units penicillin (intramuscularly) given every three hours. For the first six days 30 c.c. of 50 per cent magnesium sulfate also were given every four hours by mouth. Saline compresses were applied to the legs. The blood nonprotein nitrogen rose to 138 mg. per cent the day after admission but fell gradually to 42 mg. per cent by the sixth day. The blood pressure was reduced to 100/70 mm. by the sixth day. On discharge from the hospital on September 1 (eleventh hospital day), the urine contained a trace of albumin, 15 to 25 red blood cells, many white blood cells, and 1 to 2 granular casts.

DR. J. G. ROBBINS.—M. M. N., a 6-year-old Negro boy, was first admitted to Duke Hospital on Aug. 8, 1946, with a history of generalized swelling of four months' duration. The family history was negative. The past history revealed

From the Departments of Pediatrics, Medicine and Pathology, Duke University School of Medicine and Duke Hospital, Durham, N. C.

that he had had asthma for three years, and that four months prior to his admission here, during an asthmatic attack, slight periorbital edema developed. Shortly afterward the edema became generalized and the patient was hospitalized in a South Carolina hospital, where the edema completely subsided in seventeen days. He was then asymptomatic for three months, which period was followed by generalized edema, oliguria, and the passage of dark red urine.

On his first admission here, on Aug. 8, 1946, the temperature was 37° C. (98.6° F.), pulse 116, and blood pressure 115/70. The patient was markedly edematous from his toes to his nipple line, and his face and eyelids were similarly affected. The abdomen was markedly distended. A fluid wave and shifting dullness were demonstrable. Both lung bases were dull to percussion. The hemoglobin was 10.7 Gm., WBC 6,150, and the differential 61 segmentals, 3 stab cells, 2 J's, 25 small lymphocytes and 9 eosinophiles. There was no sickling of the red blood cells. The urine on admission had a specific gravity of 1034, 4+ albumin, 15 to 20 white blood cells and 3 to 4 granular casts, but no red blood cells in a centrifuged specimen. The stool examination and the tuberculin (0.1 mg.) and Schick tests were negative. The blood nonprotein nitrogen was 72 mg. per cent, urea nitrogen 53 mg. per cent urea ratio 73.1, uric acid 7.6 mg. per cent, total proteins 4 Gm., with 1.2 Gm. albumin and 2 to 8 Gm. globulin and the albumin-globulin ratio 0.42. The initial cholesterol was 720 mg. per cent. The heart and lungs were negative by x-ray.

The patient was placed on a high protein and low salt diet. On his third hospital day he was given 200 c.c. of plasma intravenously and the same or slightly larger amounts of plasma eleven more times during his hospital stay. Theobromine was given without effect. Paracentesis was performed on three occasions to remove abdominal fluid. Modified Southy tubes were used, one in each foot, with the removal of much fluid. During his stay, diarrhea developed, and penicillin and sulfadiazine were given. Stool cultures were negative for pathogens. The edema, urinary albumin, casts, and occasional red blood cells gradually decreased, though the white blood cells persisted. The patient's weight on admission was 37 kg. (81.4 pounds); at the end of two weeks it was 34.2 kg. (75.2 pounds); and on discharge on Oct. 5, 1946 (fifty-eighth hospital day), was 27 kg. (59.4 pounds). On discharge, the blood nonprotein nitrogen was 26 mg. per cent; total protein 3.7 Gm., albumin 2.1 Gm., globulin 1.6 Gm., and albumin-globulin ratio 1.3. There were only traces of urinary albumin.

Except for persistent albuminuria and a cold in November, 1946, the patient was well until July, 1947. Then a cold was followed by puffiness of the eyelids, swelling of the abdomen, and marked exertional dyspnea. One week before this admission on Aug. 27, 1947, severe scrotal and penile edema and marked oliguria (one to two times per day) developed. The urine frequently was dark red. The patient gained 3 kg. in weight during the three weeks before admission. When he was readmitted to Duke Hospital on Aug. 27, 1947, he presented the same physical abnormalities as on his first admission. The lung bases were markedly elevated bilaterally. The hemoglobin was 14.6 Gm. (94 per cent), W.B.C. 12,400, R.B.C. 4.4 million, the differential 3 segmentals, 4 stabs,

4 J's, 4 per cent large lymphocytes, 3 per cent S.L., 6 eosinophiles and 2 monocytes. The urine specific gravity was 1,040, albumin 4+, sugar 0, many white blood cells and hyaline and granular casts, but no red blood cells. The sedimentation rate, corrected, was 34 mm. in one hour. The blood nonprotein nitrogen was 33 mg. per cent; total protein, 4 Gm. per cent; albumin 1.7 Gm. per cent; globulin 2.3 Gm. per cent; albumin-globulin ratio 0.73. The patient was given a diet of dialyzed (sodium-free) milk.

DR. W. C. DAVISON.—The first patient is a typical example of acute glomerular nephritis. This condition represents 57 per cent of the albuminurias in children. It is characterized by hematuria, albuminuria, and cylindruria, with or without edema, hypertension, and increased nonprotein nitrogen. Respiratory infections usually precede the onset, which generally is sudden, but in this patient, as well as in two similar ones now on Howland Ward, impetigo was the precipitating infection. The first symptoms, as in this patient, are anorexia, headache, backache, and drowsiness. Fever, chills, tachycardia, dyspnea, nausea, abdominal pain, and convulsions also may occur.

Treatment.—During excessive albuminuria and hematuria, the patient should be kept in bed. Food and fluid may be reduced for the first two or three days, and if edema is marked, the salt intake should be low. After these signs have diminished, even though they persist, the patient may be allowed restricted exercise. All foci of infections (sinus, etc.) should be sought and treated, but tonsillectomy is inadvisable during albuminuria; it does not prevent nephritis, but may predispose to it. Sulfa therapy may cause improvement in acute nephritis, but as it also may damage the kidneys and cause fatal anuria, it should be used only in small doses with alkalies and forced fluids. Penicillin may be helpful. If blood transfusions are necessary for anemia, they should not be given until the urine is alkalinized by oral sodium bicarbonate or ⅙ molar sodium lactate; they may increase edema. In nephritis of less than four months, the diet should be low in protein without added salt, and in chronic nephritis the diet should contain 3 Gm. protein per kilo of ideal body weight. The usual fluid intake should be maintained. If the blood pressure is over 120 mm. or is rising, and the patient has headache, visual disturbances, coma, or convulsions (pseudo-uremia) in the course of acute glomerular nephritis, 30 to 60 c.c. (oz. i-ii) 50 per cent magnesium sulfate should be given by mouth or rectum and repeated every four hours for two to three days, *or* 5 to 10 c.c. sterile 25 per cent solution (crystalline) (0.5 c.c. per kilo of body weight; 0.2 c.c. per pound) intramuscularly and repeated two hours later if the blood pressure does not fall, *or* 2 per cent solution of the hydrated salt ($MgSO_4 . 7H_2O$) intravenously at the rate of 2 to 3 c.c. per minute, until the blood pressure falls and the coma or convulsions disappear (10 c.c. per kilo of body weight [4 c.c. per pound] may be required). Blood pressure determinations every fifteen minutes are necessary during intravenous magnesium sulfate therapy, which should be stopped when the blood pressure falls. Ten to 20 c.c. of 10 per cent sterile calcium gluconate must be available to treat a sudden fall of blood pressure or pulse. Artificial respiration may be necessary.

Prognosis.—Good; 90 per cent recover, but 28 per cent may have recurrences. In 6 per cent, the condition becomes chronic, usually in patients whose onset has been gradual; they terminate in true uremia, usually with anuria.

The second patient is a typical example of nephrosis or tubular or lipid nephritis, which causes less than 1 per cent of the albuminurias of childhood. It is a distinct clinical entity in children at the onset, which usually is gradual, and is chiefly characterized by edema and albuminuria without hematuria. As the condition progresses, glomerular and interstitial kidney changes occur. Preceding infections are less frequent than with glomerular nephritis, though it may follow URIs, malaria, poisoning, etc. The edema may subside within a few days, the albuminuria markedly diminishing and occasionally disappearing spontaneously; more usually, however, the edema may persist several weeks before disappearing, only to reappear weeks or months later. Some patients have several exacerbations over a period of years. Hypertension and hematuria, which are rare, increase the gravity of the prognosis.

Treatment.—Nothing but sodium-free (dialyzed) milk and the usual vitamins should be given for the first few weeks. Lonalac is a satisfactory preparation and the amount should be sufficient for the caloric needs. After the edema recedes, sodium-free bread, eggs, salt-free vegetables and small amounts of meat may be added. Abdominal paracentesis may be necessary, but the needle should puncture the peritoneum at a distance from the skin insertion to prevent leakage. Measles temporarily reduces the edema. Penicillin and sulfatherapy are necessary if peritonitis, skin, and other infections occur.

Unproved Remedies.—High and low protein diets, antuitrin-G, B-complex, liver extract, mercurial and xanthine diuretics, pitressin, riboflavin, thiamin, thyroid, urea, $CuSO_4$, KNO_3, NH_4NO_3, $MgSO_4$, and intravenous acacia, albumin, amino acids, blood, dextrose, globulin, plasma, and serum.

Prognosis.—Poor; recurrences are frequent and the mortality is 60 per cent. However, the patient may completely recover, even after several recurrences.

The third type of nephritis, the interstitial variety, usually is an end stage of repeated attacks of pyuria (pyelonephritis). It also may follow bacteremia, diphtheria, scarlet fever. There is no accepted treatment, and the prognosis is bad.

Dr. Walter Cargill.—A new approach to the problem of nephritis is offered by studying kidney function, by means of the clearances of various substances, such as the urea clearance, inulin clearance, diodrast clearance, etc. The "clearance" of a given substance is the volume of blood which is "cleared" of that substance by the kidney per unit of time. It may be expressed by the formula: $C = \frac{U\,V}{P}$ in which C is clearance (cubic centimeters per min.), U is the concentration in the urine (mg. %), V is the rate of urine flow (cubic centimeters per min.), and P the plasma level (mg. %).

Since certain substances are handled by the kidney in a particular fashion, their clearances have unusual significance. For example, inulin is a complex polysaccharide which is excreted solely by glomerular filtration; that is, it is

neither excreted nor reabsorbed by the tubules. The amount of inulin which is "cleared" from the blood per minute depends entirely on the amount of plasma which is filtered through the glomeruli per minute; therefore, the inulin clearance is, for all practical purposes, the same as the rate of glomerular filtration. Other substances, such as diodrast, phenolsulfonthalein, and sodium para-aminohippurate (PAH) are excreted almost entirely by the cells of the proximal convoluted tubules. This excretory mechanism works with great efficiency, so that at low plasma levels, diodrast and PAH are completely removed from the blood in one passage through the kidney, and the only limitation to the amount of these substances which can be excreted is the amount of blood which passes through the kidney. The clearance of diodrast or PAH indicates, therefore, the minimum rate of plasma flow through the kidney. Since only the plasma which perfuses functional tubular cells can be measured in this way, the clearance of diodrast or PAH is equal to the effective renal plasma flow, and does not measure the total circulation through the kidney. The normal value for this clearance is so high, however (about 690 c.c. per minute), that the total flow cannot be much greater. It may be expressed: $C_D = C_{PAH} = RPF = 690$ c.c. per minute.

This excretory mechanism which works with such great efficiency at low plasma levels can be overloaded by raising the plasma concentration. If the excretion of diodrast is plotted against a rising plasma level, the excretion increases in a straight line to a certain point, at which it levels off and does not increase further, no matter how high the plasma concentration. At this point of maximal excretion the mechanism for the transfer of diodrast across the cell is saturated, and this saturation level is known as the diodrast T_m (transfer maxima). When all of the tubular cells are saturated, that is, excreting maximally, the amount of diodrast which can be excreted depends entirely on the number of tubules excreting. The diodrast T_m is, therefore, a measure of the total number of functioning tubules, or of the tubular excretory mass. T_mD = Maximal Excretion = 40 mg. per minute = tubular excretory mass. The same is true, of course, for PAH, except the average normal value is 78 mg. per minute.

A study of twenty-two nephritis patients by these methods[1] indicated that the anatomical term "glomerulonephritis" is not entirely correct, since even in the earliest stages of acute nephritis, the tubular function also is impaired. That the damage is predominantly glomerular, however, is borne out by the finding of a greater impairment of glomerular function, that is, filtration, than of tubular excretion. The ratio $\frac{F\,R}{T_mD}$ was found to be low, as was also the filtration fraction $\frac{F\,R}{RPF}$, indicating that there was greater impairment of filtration than of circulation through the kidney. This fits in very well with the pathologic findings in this stage of the disease.

In the later stages of nephritis, all of the functions studied (FR, RPF, and T_mD) showed a parallel fall, although the low ratio of glomerular function to tubular function remained. Diastolic hypertension did not regularly develop unless there was a marked decrease in tubular excretory mass, reflected in a fall

of T_mD to 20 mg. per minute or less. These functional studies have failed to reveal a distinct difference between nephritis and nephrosis.

Edema formation is closely related to the retention of salt. Salt is normally filtered by the glomeruli and almost completely reabsorbed (98 to 99 per cent) by the tubules. It is conceivable that if the filtration rate is reduced while the tubular reabsorption is relatively unimpaired, there will be a tendency toward retention of salt. Conversely, if there is greater damage to the reabsorptive mechanism than to filtration, there will be a net loss of salt. Some such disturbance in the functional organization of the nephron may be the basis for the distinction of the clinical types of nephritis.

DR. BERNARD BLACK-SCHAFFER.—Glomerulonephritis is an inflammation of the kidney. Regardless of the etiology of the lesion, the basic pattern is similar to all inflammation. Examination of a section by a student may not lead to a positive diagnosis in most instances, because acute glomerulonephritis is frequently characterized only by minimal increased cellularity of the tufts. Such an increase commonly is due to an accumulation of polymorphonuclear leucocytes and a proliferation of the endothelial cells of the capillaries. In common with all inflammatory lesions, the degree varies from minimal to maximum. The example of nephritis presented by the first patient would be represented by minimal lesions. Since a fatal outcome is most uncommon, it is difficult to illustrate the above statement with histologic material. While it is true that the structure most prominently involved is the glomerulus, the proximal convoluted tubules are involved. Not infrequently in severe cases hematuria is pronounced. In such instances, the kidneys, when examined, reveal, in addition to the simple changes described above, hemorrhage from the capillaries of the tufts, producing what has been called hemorrhagic nephritis. This nephritis does not differ from the nephritis described above, but is merely an expression of greater capillary damage. As in all inflammatory processes, healing may occur in glomerulonephritis. Where minimal damage was produced, the healing process is complete and no residuum remains. On the other hand, where the damage is more severe or progressive, irreversible changes may occur, resulting in so-called subacute and chronic glomerulonephritis, with ultimate kidney failure.

Nephrosis is a problem which has raised a controversy between the pediatricians and the pathologists. Pediatricians, on one hand, consider nephrosis to be an entity divorced from glomerulonephritis. Pathologists, on the other hand, basing their conclusions on autopsies of patients who have died after repeated exacerbations of nephrosis, have decided that it is only a stage of glomerulonephritis. However, the rare autopsies on patients who have died early in the course of nephrosis show that the tubules are more markedly implicated than the glomeruli and interstitial tissue, although they, too, are damaged.

REFERENCE

1. Earle, D. P., Jr., Taggart, J. V., and Shannon, J. A.: Glomerulonephritis. A Survey of the Functional Organization of the Kidney in Various Stages of Diffuse Glomerulonephritis, J. Clin. Investigation 23: 119-137, 1944.

Psychologic Aspects of Pediatrics

GLUTAMIC ACID AND MENTAL FUNCTIONING

HARRY BAKWIN, M.D.
NEW YORK, N. Y.

IN 1943, Price, Waelsch, and Putnam[1] reported that the administration of glutamic acid to patients with petit mal and psychomotor attacks led to an increase in mental and physical alertness. The degree of improvement in mental efficiency could not be correlated with the decrease in the number of seizures. The treated patients appeared to be happier and more congenial. Mood swings were less pronounced and behavior mannerisms were ameliorated.

These findings were not anticipated. Glutamic acid was tested in epilepties because it yields free acid which, it has been suggested, is anticonvulsant. Furthermore l-glutamic acid is the only amino acid known to be metabolized by slices of brain tissues.

Zimmerman and Ross[2] observed significant differences in maze learning between white rats fed glutamic acid and a control group, the treated group mastering the maze in less than half the time taken by the controls.

Albert, Hoch, and Waelsch[3] were able to raise the level of mental functioning in seven out of eight mentally deficient patients with total daily doses of 8 to 10 Gm. of glutamic acid.

More recently Zimmerman, Burgemeister, and Putnam[4] reported the results of glutamic acid therapy upon mental functioning in children and adolescents of various intellectual levels (Intelligence Quotients ranges from below 30 to 131). Using a wide barrage of tests, they found that glutamic acid accelerates mental functioning generally as indicated by verbal, motor, and Rorschach tests. The most striking changes were observed in the seriously retarded group. The average increase was about seven points on the Stanford Binét test. In two children the Intelligence Quotient rose 16 and 18 points, respectively.

The efficacy of glutamic acid depends on its continuous use. Its favorable effects disappear quickly when it is discontinued.

Glutamic acid may be administered in tablet, capsule, or powder form. It is dispensed in 0.5 Gm. capsules and tablets. It may be incorporated in the food. It is best given at the end of the meal or immediately afterward to minimize gastric distress. A suitable initial dose is 2 Gm., three times a day. The amount is increased gradually to the point where there is overactivity and distractibility and noncooperativeness of the child. When these manifestations appear the dose is gradually decreased. Occasionally there is insomnia. In such instances the last dose of the day is given in the later afternoon instead of at bedtime.

From the Department of Pediatrics, New York University, College of Medicine.

The effective dose varies widely and bears no relation to age. It ranges from 6 to 24 Gm. a day. In most instances, the larger doses are necessary in order to obtain an effect. Where there is gastric distress the dose is reduced until the symptoms disappear and then gradually increased to an effective level; or the glutamic acid is discontinued for a few days and then gradually increased as tolerance develops.

The clinical usefulness of glutamic acid is being actively investigated and more information about its clinical application will soon be available. It promises to be helpful in the treatment of children with retarded or borderline mentality where the rise of a few points in the Intelligence Quotient leads to an appreciable improvement in the child's performance at school and a bettering of his ability to cope with his school-fellows.

By encouraging the parents, it may be expected to improve parent-child relationships, thereby lessening emotional disturbances which so often exaggerate the plight of the slow child.

REFERENCES

1. Price, J. C., Waelsch, H., and Putnam, T. J.: dl-Glutamic Acid Hydrochloride in the Treatment of Petit Mal and Psychomotor Seizures, J. A. M. A. **122**: 1153, 1943.
2. Zimmerman, F. T., and Ross, S.: Effect of Glutamic Acid and Other Amino Acids on Maze Learning in the White Rat, Arch. Neurol. and Psychiat. **51**: 446, 1944.
3. Albert, K. E., Hoch, P., and Waelsch, H.: Preliminary Report on the Effect of Glutamic Acid Administration in Mentally Retarded Subjects, J. Nerv. and Ment. Dis. **104**: 263, 1946.
4. Zimmerman, F. T., Burgemeister, B. B., and Putnam, T. J.: A Group Study of the Effect of Glutamic Acid Upon Mental Functioning in Children and Adolescents, Psychomatic Med. **9**: 175, 1947.

The Social Aspects of Medicine

NOW IS THE TIME

A Proposal Concerning Prepayment Medical Care

Walter A. Noehren
Vancouver, Wash.

The development of a medical care program in this country has made considerable progress in the past decade. Progress is too slow however, and we are constantly threatened by possible revolutionary changes in medical care such as are proposed in some of the present bills before congress. It is clear that a change will come and that the time is short. It is disappointing to realize that the American Medical Association has fallen into the role of conservative moderator in this problem. The present attempts to provide care by voluntary prepayment plans cannot solve many of the basic aspects of the problem. The present American Medical Association program (1) will not reach low or indigent income groups, (2) will not give complete care, (3) is proving inefficient, (4) does not pay the full cost of hospitalization, (5) is not creating adequate facilities, (6) does not support research, and (7) is not reaching rural and sparsely populated areas.

The American Medical Association, if it wishes to control medical practice in this country, as it certainly does and as is proper, should develop a more comprehensive approach to the problem now. A step forward must be found which will further progress, yet which will allow physicians and patients their proper relationships. The following proposal suggests one possible method of accomplishing this. The proposal is:

That each individual in the country would be required by law to pay, each year, a sum adequate for his complete medical care. He would pay this to a prepayment medical care plan which exists in his area and which is properly incorporated as a nonprofit organization. Those unable to pay such a fee would apply for payment in whole or in part of this fee by government to a medical care plan selected by the individual. These latter persons would be, for the most part, those who are now receiving government care through welfare agencies, but might include also the very low income groups. Evidence that such payment had been made for the current year would be required by the Bureau of Internal Revenue at the time of income tax declaration. Government agencies would not directly handle funds except for those unable to pay. This method of required prepayment would be roughly comparable to present methods of payment of automobile liability insurance in states where such insurance is required by law.

The laws of incorporation for prepayment plans would be broad enough to allow all of the forms of prepayment plans which now exist except for those which are run for profit. Such plans would include: (1) those of the medical societies, which are a form of producer cooperative; (2) those run by physician groups but not necessarily under medical society sponsorship; (3) those of nonprofit corporations or foundations, and (4) those which are consumer cooperatives. All of these types exist at the present time and in some areas there is already a wide choice available between various prepayment plans, although almost none offer complete care. The plans should necessarily, to accomplish their full purpose, cover all aspects of medical care including hospitalization.

Under such a proposal, the total amount of money spent in this country for medical care would be only as much more as would be required to produce the

extension of care which is demanded by modern standards. That modern medical care should be available now to all people is beyond question. Each individual would have to pay his annual fee, which would be sizable, but he would derive manifest benefits in return. Many people have already chosen to pay a portion of this fee voluntarily and would welcome the increased efficiency which would result from the extension of the insurance principle to the entire population. The private practice of medicine would continue as at present and any person could seek private care at any time with the exception that he could not seek such care from any physician on the panel of his chosen prepayment plan. He could seek such care from physicians on the panels of other plans, or from physicians who would wish to do private practice only. The only fundamental change which would occur in medical practice would be that fewer patients would seek private care since they would have prepayment care by a physician group of their own choosing available to them. The American Medical Association has already endorsed this principle however, and no other group, except profit groups, could object to such a change. There should be general agreement that medical care should never be conducted with a profit motive. Certainly an intermediary third party, even in the form of an insurance carrier, should never profit from medical care.

Should such a proposal as this be effected, a variety of changes would occur in the present management of medical care. It would seem that the whole evolution would favor the medical profession immensely.

The present wishful thinking about preserving the individual physician as an isolated practitioner would immediately cease, and the medical profession would have to cooperate among themselves in the necessity of proving their contention that medical care should be administered by physicians and not by lay individuals or by government. Because of the complexity and specialization in modern medical care, it is becoming clear that a physician can no longer practice as an isolated individual. Even the general practitioner is becoming a highly trained specialist who must have ready access to experts in a wide variety of fields to give his patients adequate care. He cannot practice alone, but must be part of a group. Such a group can be as small as five or ten men, or it can be considerably larger. It can be closely organized, or can be a more loose relationship. The medical societies themselves, which exist as county units, are essentially groups, and when such societies sponsor prepayment plans, the physicians on the panels of the plans are working as groups. Failure to realize this fully has been the major fault of the medical society prepayment health plans, for in these plans the physicians are often selfish in the use of prepayment funds. A physician may order laboratory studies or prescribe therapy which is extravagant and even of questionable value to the patient, or he may see a patient more often than is necessary, and thus use up funds needed for the care of other sick patients. He is thinking in terms of his individual patient and of his individual fee for service without giving proper recognition to the fact that he is one of a group of physicians attempting to provide care to a larger group of patients. The result of this has been an inefficiency which has made it necessary for the medical society prepayment plans either to charge higher fees or to reduce their coverage to the point where the plans have value only for serious or emergency illness.

All of the physicians on the panel of any prepayment plan must work together as a group so that they can give care where it has real value. This may seem to be compromising the judgment of the individual physician toward his individual patient, but this same compromise always exists in the patient-doctor relationship, except in the treatment of the very wealthy. In private practice the physician cannot order laboratory studies or hospitalization at will, because patients are often unable to pay for these, or because there would be no money

left to pay the physician's fee. Medical care is very costly at best, and must be given with economy. Under whatever system, voluntary or compulsory, the medical societies must fully realize this point before prepayment care can succeed. In addition, a considerable education of the general public is required, for many patients attempt to misuse prepayment, largely through misunderstanding. Patients must be reasonable in requests for care, and they must be educated in this reasonableness by the medical profession.

Among the outstanding medical groups in the country are the medical school faculties. A few of these at present are developing participation in prepayment plans. Many others are talking about doing so. The university groups today are faced with problems which will need solution soon. Because of diminishing income from endowments, there is a real need for more money. Because of dependence on indigent patients for teaching material, there is need for more patients in periods of prosperity such as was experienced during the war, and which we all hope may be achieved in peace time. Under a plan of required membership in prepayment plans, as suggested, the university physician groups could organize as prepayment groups and because of their great prestige, would attract a large patient clientele. They would actually tend to dominate the practice in some areas. This would be proper and in keeping with their excellence. Each might be part of a medical society plan, or might compete with a medical society plan. In any event, the university groups would receive a large income from their work, and would have an increased patient load consisting of patients who, by their joining a university plan, would have expressed their willingness to be used for teaching purposes. It has been well shown that most people do not object to this, but recognize its advantages to them as patients. Students and physicians in training would then deal with patients on a proper level.

The present county, city, and charity hospitals would change their status completely under the proposed plan of required prepayment insurance. These facilities would become, in fact, private hospitals and would accept staffs suitable to their board of directors. There would no longer be the charity or welfare patient, which would be a blessing for all concerned. The inadequate care which patients now receive in many isolated and understaffed county hospitals would be improved because of increased physician economic interest in these patients.

Under a plan of required membership in prepayment plans, as proposed, no physician group would ever be able to relax in its efforts to do good work. The public in the course of time will be an even better judge of medical care, and will express this judgment in its choice of prepayment plan. Monopolization of prepayment would be very unlikely, since groups as small as ten men would be able to form prepayment plans would could effectively compete in the field. Smaller groups would have to refer some of their more specialized work, such as neurosurgery, to larger centers and would pay fee-for-service for such work.

The individual patient could be given the privilege of changing groups, but he should not be allowed to do so more than once in a given period of time without special justification. To shop from doctor to doctor is poor and an extravagant way to seek medical care. This shopping about is too frequently indulged in under present medical society plans.

The supplementary use of private consultants would occur and has been experienced under some of the already existing prepayment plans, where it fills an excellent role. Occasionally, in the case of serious illness, the patient or his family feels the desire for further opinion. The group caring for the patient under prepayment considers the care already being received completely adequate, but does not object to further opinion. The family, having no expense for the illness, since it has been provided for under prepayment, is able to afford even sizable consultant fees. The consultant is called in and the situation benefits from this added, though usually unnecessary, opinion.

The phrases "freedom-of-choice of physician" and "fee-for-service" concerning which many physicians argue vehemently in current discussions of medical care, would be properly tested under such a plan as the one proposed. "Freedom-of-choice" is at best a relative thing and must be understood in its relationships to the number of physicians in an area, proper training for various specialized functions, ability of patients to choose a proper physician, and ability to pay. Certainly as much "freedom-of-choice" as can be obtained is desirable. Under present circumstances, a large portion of the population has exceedingly limited choice and many have no choice. It is a challenge directly to the medical profession to improve this situation both by making this freedom truly available and by educating the public to the ability to choose. Under this proposed plan of required insurance, each person would be able to choose a group, and even to choose a "family doctor" by selecting a prepayment group which would make a physician of his choosing available to him. The individual would further be able to change his group at least once in a time period, and he could always seek private care at his own extra cost. What further "freedom-of-choice" the medical profession would desire for their patients, they would have to provide and prove valid in group competition. It would not be possible to make allowance for extravagant misuse of "freedom-of-choice" and "fee-for-service" by cutting back on coverage or by other schemes such as indemnity plans, since complete coverage at proper over-all fee would be required of them. What the proper over-all fee would be could be determined accurately in the course of time by the competition between the various prepayment groups, and could be controlled properly by the medical profession. The profession's chance of achieving this proper income level may well depend on its ability to produce a real solution to the medical care problem before some revolutionary and irrevocable scheme is hoisted upon it.

Under the proposed plan of required prepayment insurance, the status of various types of hospital administration would not have to change at first, but one would expect an evolution of ownership and directorship of hospitals by the prepayment corporations which would give the advantage of increased efficiency with closer control of all hospitals by physicians. The fact that hospitals would be controlled by specific groups would not mean that other physicians need be excluded any more than under present methods of hospital control. The Permanente Foundation hospitals for example, which are run by physician groups who give prepayment care, are open staff hospitals and are used by other physicians of the areas for private patients. All physicians associated with prepayment groups would automatically have proper hospital relationships and privileges. This would directly solve the difficulties of the general practitioners who would realize their full importance in prepayment care.

The present status of hospitalization under medical society voluntary prepayment plans contains faults of which many are not aware. Most of the plans are content to extend limited hospital coverage usually under a separate contract with Blue Cross. The medical profession prefers to concern itself only with medical practice and is happy to have someone else worry about hospitalization. Even now, 70 per cent of the hospital beds in this country are in government control. Yet medical care and hospitalization are inseparable by modern standards and both should be controlled properly by the medical profession. The particular fault of present hospitalization insurance is that it is not adequate to pay for what it attempts to provide, since it depends on private patient income, on hospital endowments, and on government funds to pay much of the costs. If voluntary prepayment succeeds as well as the American Medical Association hopes it will, the private patient hospital income will diminish. Endowment is becoming increasingly scarce. Government subsidy of hospitalization must then become increasingly important. New facilities will be created

only with government help. This phase of medical care can become as unhappily involved in politics as can the practice of medicine itself, and it can interfere considerably with the practice. In its attempts to preserve its own dignity, why does the medical profession lean so heavily in this respect on government and on Blue Cross, a lay corporation? The unity of medical practice and hospitalization must be realized.

Under the proposed plan of required prepayment insurance there would be no excuse for further extension of public health administration into general medical care, and in some fields already invaded, this work could revert back to the practicing physicians where it belongs. Public health administration should continue more or less as it now exists, but should be made available in all areas. All problems of clinical medicine, however, should be handled by the practicing physicians. The public health authority should limit its activity to such work as study of epidemiologic data, enforcement of therapy as prescribed by law, sanitation, pest control and the like. A closer unity of purpose could be achieved in public health since the health authorities would be dealing with physician groups rather than with a large number of individual physicians. Reporting of infectious disease, poorly done by individual physicians, could be accomplished better through groups. Economic want would never interfere with adequate therapy. The medical profession should welcome a means of stopping the broadening powers of the public health authority, and the public health authority should be happy to be able to administer an effective program without the need to indulge in actual medical care. In a few specialized fields now well established, it might be desirable to continue governmental administration, as in tuberculosis and in mental illness.

The care of veterans, under the proposed plan, could be accomplished by having the government pay the prepayment fee for nonservice connected care of the veteran to a physician group of the veteran's choosing. Service-connected disabilities could be handled as at present, either in veterans' hospitals or by special contract with practicing physicians. The huge new veterans' hospitals might better be general community hospitals staffed by local physicians rather than by straight government employees.

Under this proposed plan of required prepayment insurance, the role of government would be limited even more than it is at present, since all welfare care would be placed back on a patient-physician relationship, government ownership of hospital facilities would be reduced, and public health authority would be limited. The role of government would be limited to writing the laws regulating prepayment corporations (as is done under voluntary plans), arbitration of these laws, investigation of individual income as concerns ability to pay for medical care (as is done for income tax and for present welfare care), and distribution of tax-raised funds to medical prepayment corporations, but always to the corporation selected by the individual citizen, free of political pressure. It is difficult to see how a government bureaucracy could evolve under this type of control, or how politics could have much influence.

The competitive profit motive in medical practice could be fully maintained, just as in voluntary plans. A large new source of income to physicians would accrue from the establishment of regular fees for patients now treated for substandard welfare fees or as charity patients.

Should such a proposal be effected, it would not be an irreversible move, but could be discontinued with a return to present status. The final outcome of such a plan would depend almost entirely on the ability of the medical profession to produce good care economically and in a form satisfactory to patients. If the physicians themselves failed in their administrative functions, they would possibly become the servants of consumer cooperatives. It is most likely, however, that consumer cooperatives would fall by the wayside because of their

indirectness. It is proper that medical care should be administered by physicians, not by physicians sitting in regional or national offices, and certainly not by physicians in government employ or in the cabinet, but by the physicians who are doing the actual competitive practice of medicine.

Under a proposal such as this, there would be no basic change in the present status of physicians except for their admission that they practice as groups and not alone. They would have all the patients, plenty of money, and the ability to create proper modern facilities in all areas. In sponsoring voluntary prepayment plans, the physicians have already endorsed the group principle. To hope that voluntary prepayment will solve the medical care problem in this country is unrealistic, even if it may seem the lesser of evils. A middle ground of sound principle must be found. It must be endorsed by the medical profession, and it must be soon.

Sept. 8, 1947

Dear Doctor Park:

Congratulations to you and to Dr. Veeder on publishing the Canadian Medical Association's "Submission Respecting Health Insurance" of 1943. The flexibility, the decentralization, the recognition of *inadequacy of distribution* of medical care, the obvious desire of the Canadian Association to *learn* and to cooperate with measures "not contrary to the public interest," indicate the social maturity that group has attained.

In your introductory note, you inquire plaintively, "Why then should they think so differently from us?" Why indeed?

I came across what seems very close to the right answer in a masterly editorial in the *Buffalo Evening News* of Aug. 1, 1947:

"While friend and foe join in recognizing the United States as the most powerful country on the face of the globe, many couple this admission of our strength with the charge that we are so immature mentally that we don't know how to make wise use of our power."

The writer of the editorial quotes with approval Dr. Bernard Iddings Bell's praise of the American college and university for producing competent technicians and reprehends them for failing to produce "human beings competent to live," citing Sir Richard Livingstone's definition of a technician as one who "understands everything about his job except its ultimate purpose and its place in the order of the universe."

The editorial closes with the admonition to our educational institutions to put further emphasis on ideas, moralities, philosophies, and faiths, in order to speed the *maturity of the Common Man.*

Now, Dr. Park, all this applies especially to us physicians, both young and old. Indeed, I am quite sure it is the reason your Column exists. Throughout medical school, internship, research, or practice it is so tremendously difficult to acquire, to keep up with, and to practice medical technology, that all too many competent physicians are socially and culturally the merest tyros. The recent, wartime acceleration, abridging premedical cultural training, eliminating intramedical vacations, has helped not at all. Even the pediatrician, whose very work partakes of preventive medicine, and sociology, not to mention politics, is in neither the Waltonian nor Davisonian sense *compleat,* if he has not looked to the acuteness of his social conscience.

The fact that we physicians have some excuse in our unremitting toil for a degree of extramedical immaturity, by no means confers adequate absolution. To whom so much is given, to him shall much be required. All too well do we deserve the rebuke given the complacent Pharisees: "These ought ye to have done and not to leave the other undone!"

PARK J. WHITE, M.D.

Comments on Current Literature

INFECTIOUS DISEASE IN PREGNANCY AND FETAL MALDEVELOPMENT

BIOLOGISTS and clinicians alike have recognized for many years that two main mechanisms are involved in abnormal development: intrinsic abnormalities of germinal origin, and those abnormalities which are produced by external influences upon essentially normal ova.

As early as 1909 Stockard[1] made the following salient remarks:

> The well-known congenital defects of the heart and other parts of the vascular system, digestive tract, as well as the numerous developmental arrests in various parts of the body, remind the observer of the great loss in ability that the race suffers as a result of faulty development. These defects in construction must be considered a disease which causes death of about 23 per cent of the human race before or shortly after the time of birth, and handicaps a certain proportion of the survivors throughout their lives. We carefully study and use all known precautions to protect ourselves against post-natal infections and diseases, and much interest and time is given to combating the causes, yet little is said and scarcely anything done toward a control of development or the hygienic protection of the developing individual.

However, it remained for Gregg[2] through studies of rubella in pregnancy, to make clinical application of the discoveries of pioneers in this field, notably, Stockard and Mall. Gregg in 1941 first reported the relationship between rubella in the pregnant woman and congenital abnormalities in children. The most commonly noted defects are congenital cataract and other ocular effects, malformations of the heart, and microcephaly and mental retardation. Less common effects which have been noted are hydrocephalus, deafness and deafmutism, and cryptorchism. Since 1941, a large number of cases of congenital abnormalities associated with maternal rubella have been reported, approximately 500 according to Ingalls,[3, 4] the majority of these being discovered by the investigation of pregnancies which resulted in defective infants.

While these reports are of considerable interest, it has been emphasized recently that "the existing need is for further exploration of the causes of abortions, monstrosities, and congenital anomalies through correlated epidemiologic, clinical, and teratologic studies."[3]

Ober, Horton, and Feemster,[5] in a recent report dealing with congenital defects in a year of epidemic rubella, approached the rubella problem from an epidemiologic point of view. Of 35,000 cases of rubella reported in this 1943 epidemic, which was at least twice the usual incidence, 3,000 cases occurred in females in the age group 17 to 49 years. Response to a survey by mail of the reported cases in females yielded the following information: of the 1,164 women who responded to the questionnaire, 438, or 38 per cent were married at the time of their infection; forty-nine, or 11 per cent of the 438 who were married were pregnant when they had rubella. In addition, five cases of rubella during pregnancy occurred in years other than 1943, making a total of fifty-four cases. Of five women who had rubella during the first month of pregnancy, two aborted, two had defective infants, and one had a normal infant; thus, 80 per cent of infants in this instance were either lost or defective. Where the infection occurred in the second month of pregnancy, 50 per cent of the infants were lost or defective: of eight infants, two were stillborn, two were defective, and four were normal. In the third month of pregnancy, two abortions and one defective infant were recorded with six infants normal, or 33⅓ per cent of the infants lost or defective; with rubella in the fourth month, of five instances, three

infants were normal, one was an abortion, and one was defective, an incidence of 40 per cent lost or defective. Statistics in this epidemic on the remaining months of pregnancy revealed the following: one minor defect in the sixth month, two stillbirths, seventh and eighth months respectively, one defective infant where the month of pregnancy at which infection occurred was not known. Thus, in the fifty-four cases, there were eight defective infants and nine pregnancies which terminated in an abortion or stillbirth.

The authors refer to similar studies made by Fox and Bortin[6] and Aycock and Ingalls.[7] Stress is laid on the fact that "with the exception of Aycock and Ingalls, no previous authors have emphasized that abortions and stillbirths may result from infection of pregnant women with rubella," and that in their present survey the number of abortions and stillbirths uncovered was as large as the number of defective children. The need for further surveys is emphasized and particularly the need for comparisons made between the incidence of congenital abnormalities where pregnancy is not complicated by communicable disease and that noted where the pregnancy has been complicated by virus or bacterial disease.

The role of communicable disease in mongolism was discussed recently in a comprehensive article by Ingalls,[3] who presents data in support of the conception that mongolism originates between the sixth and ninth weeks of fetal life. According to Ingalls, the causative agents include hemorrhage, threatened abortion, pathologic abnormalities of the uterus, and certain intercurrent infections. The last category is of special interest. Ingalls and Davies[8] have reported seven instances of acute intercurrent infections observed during pregnancy which terminated in the delivery of a mongoloid infant. In six of the seven cases the particular disease occurred toward the end of the second month of gestation; one case of rubella in the first trimester of pregnancy was associated with the birth of a mongoloid child. Two additional instances of mongolism associated with maternal rubella in early pregnancy are cited by these authors, one in which rubella occurred during the third month and the other known to have occurred during the first trimester of pregnancy. In an evaluation of these data, Ingalls[3] concludes that on the basis of epidemiologic probability, "it is unlikely for the observed combination of three cases of rubella and mongolism to occur by chance."

Such critical surveys may bring about a fuller understanding of the prenatal factors which are involved in fetal maldevelopment, and may lead to a more effective control of some of these factors with consequent improvement in the hygienic protection of the developing individual.

RUSSELL J. BLATTNER.

REFERENCES

1. Stockard, C. R.: Am. J. Obst. **59**: 582, 1909. Quoted by Ingalls; see (3).
2. Gregg, N. McA.: Congenital Cataract Following German Measles in the Mother, Tr. Ophth. Soc. Aust. **3**: 35, 1941.
3. Ingalls, Theo. H.: Etiology of Mongolism: Epidemiologic and Teratologic Implications, Am. J. Dis. Child. **74**: 147, 1947.
4. Cordes, F. C., and Barber, A.: Changes in the Lens of the Embryo After Rubella; Microscopic Examination of Eight-Week-Old Embryo, Arch. Ophth. **36**: 135, 1946. Quoted by Ingalls; see (3).
5. Ober, R. E., Horton, R. J. M., and Feemster, R. F.: Congenital Defects in a Year of Epidemic Rubella, Am. J. Pub. Health **37**: 1328, 1947.
6. Fox, M. J., and Bortin, M. M.: Rubella in Pregnancy Causing Malformations in the Newborn, J. A. M. A. **130**: 568, 1946.
7. Aycock, W. L., and Ingalls, T. H.: Maternal Disease as a Principle in the Epidemiology of Congenital Anomalies, Am. J. M. Sc. **212**: 366, 1946.
8. Ingalls, T. H., and Davies, J. A. V.: Mongolism Following Intercurrent Infectious Disease in Pregnancy, New Eng. J. Med. **236**: 437, 1947.

News and Notes

Dr. Guy W. Brugler, Assistant Director of the University Hospitals in Cleveland, has been appointed Director of the Children's Hospital of Boston, and the proposed $10,000,000 Children's Medical Center. Dr. Brugler who has been with the University Hospitals in Cleveland since 1939, served with the Army's 4th General Hospital in Australia and New Guinea, and later was executive officer at the Woodrow Wilson Army Hospital at Staunton, Va. He is a member of the Senior Medical Advisory Group to the Veterans' Administration.

The **American Academy of Pediatrics** will hold the following meetings in 1948:

National Meeting.—Nov. 1-4, 1948, Chalfonte-Haddon Hall Hotel, Atlantic City, N. J.

Areal Meetings.—April 29, 30, and May 1, 2, 1948, Statler Hotel, Buffalo, N. Y., for Districts I, II, III, and IV.

June 28 to 30, 1948, Hotel Schroeder, Milwaukee, Wisconsin, for Districts V, VI, and VII.

Sept. 13 to 15, 1948, Olympic Hotel, Seattle, Washington, for Districts VI, VII, and VIII.

Poliomyelitis occurred in epidemic form in a number of European countries in 1947, according to the epidemiological Record of the Interim Commission of the World Health Organization.

In England and Wales an epidemic started early in June and by mid-August nearly 3,000 cases had been reported. The London area, the West Riding of Yorkshire, and Lancaster were the chief focal points. Some increase also occurred in Scotland. In France the reported cases were three times the median and in Austria twenty times the median. In Italy the rate remained high as it was in 1946. In Belgium where it was epidemic in 1945 the rate remained low, as it did in Denmark, Finland, and the Netherlands. In Sweden where it was also epidemic in 1945 the rate for the first half of 1947 was low. In Switzerland the high rate of 1946 continued into 1947. An increase was reported as taking place during the summer in the occupied zones in Germany.

Book Reviews

Hospital Care in the United States. Commission on Hospital Care, 1947. New York. The Commonwealth Fund, pp. 631. Price $4.50.

The Commission on Hospital Care was established in the fall of 1944 with President Thomas S. Gates of the University of Pennsylvania as chairman. Included in the twenty members of the Commission were physicians, hospital administrators, and representatives of the public, such as Herbert Hoover. Dr. A. C. Bachmeyer was director of the study staff. The work of the Commission was financed by grants from the Foundation.

The report summarizes an intensive survey of the hospitals in the United States in which it was assisted in the field work by the U. S. Public Health Service. The Commission has inaugurated hospital surveys in every state which are now under way, and selected Michigan for a pilot study. A detailed report of the Michigan survey is included in this report.

In all, the Commission makes 181 specific recommendations which are discussed in the report. These involve every phase of the hospital, as needs, organization, administration, education, nursing, medical staff. Obviously a review cannot discuss these 181 recommendations in detail. Based on its Michigan survey, the Commission finds a need for 195,000 additional general hospital beds in the United States, and finds that some 25 per cent of existing beds are outmoded. At present prices it would cost something like $1,800,000,000 for this construction. It recommends that there should be fewer hospitals than at present but larger hospitals. The responsibility of the hospital to the community should be extended to include preventive medicine and health education. Group practice with the hospital as a center should be extended where locally possible. There is need for much more integration of services and facilities among the hospitals. Facilities for the care of communicable diseases, including pulmonary tuberculosis, should be provided in the general hospital. Closer relationship should be established between the hospital and departments of public health. These are but a few of the recommendations, but they illustrate the broad viewpoint of the discussion and report. Section seven of the report devotes nearly 100 pages to an interesting history of hospitals in the United States.

In view of the widespread increased use of hospitals which has taken place in recent years, and the overcrowding that exists, together with the present enactment of federal legislation for the development of increased hospital facilities, the report is not only timely but of universal interest and importance.

B. S. V.

Let's Talk About Your Baby. H. Kent Tenney, Jr., M.D., ed. 3, Minneapolis, 1947, The University of Minnesota Press. Price $1.50.

This is one of the best and easily the most unique book on infant care for parents that has been published. It can be recommended safely by the physician, and because of the method of presentation of the advice, its educational value for the laity is greater than that of the usual, more formulized texts. Only a few changes have been made in the new edition from the previous text.

Editor's Column

DR. PARK'S CENTENNIAL ADDRESS

Through the kind permission of The New York Academy of Medicine, the JOURNAL publishes in this issue (p. 599) the address of Dr. Edwards Park on "Changing Medical Care in Our Changing National Life," given at the Centennial meeting of the Pediatric Section of the Academy last March, when Dr. Park was the guest speaker. By publication in the JOURNAL, the address will be given a larger audience than it would receive by publication in the Academy Bulletin alone, and it was for this reason that it was made available by the author and by the Academy to the JOURNAL for simultaneous publication.

The ideas and thoughts of the author reflect his own viewpoints of course, and should not be construed as reflecting the opinion of the Academy of Medicine, nor of the Editor or Publisher of the JOURNAL.

In the opinion of the Editor, it is one of the most statesmanlike discussions of the problems of medical care that has been made. Whether one agrees or disagrees in whole or in part with Dr. Park's views, one must respect his clear thinking and sincerity, and admire the tolerant, unemotional way he has presented his discussion of the present-day problems of medical care. His criticisms are essentially constructive. We hope that our pediatric colleagues will spread the news of Dr. Park's address to their friends in other fields, as it is not a discussion of pediatric problems, but of the general problems of medical care.

MEDICAL CARE AND POLITICS

A short time ago we were discussing medical care and medical economics with a newspaperman who has been a close political observer for many years, and whose comments on political matters have a nationwide audience. Some of his comments were very penetrating. His opinion was that, whether or not the doctors liked it, and whether or not it was for the best interests of medical care for the people, medical care and medical economics are, today, a matter of politics. Both political parties in the United States look upon the subject as one of major political importance, and the chief question at issue is as to which party can get the credit for medical legislation, and in this way reap political benefit. As long as one party is in executive control and the other in legislative control, as at present, we would not have much medical legislation affecting the individual directly. If either party gained control of both branches in the next election we would have federal legislation in a hurry, as the party in power would gain political credit with the people. If the Democratic party should win both branches, we could expect a Wagner-Murray-Dingell bill to be enacted. If the Republican party should win, we could expect a very much changed Taft-Hartley bill, containing many of the provisions of the bill now fostered by the Democratic legislators, made into a law.

B. S. V.

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References: 1. Dodd, K. and Minot, A. S.: *J. Pediat.*, 8:442, 1936.
2. Dodd, K. and Minot, A. S.: *J. Pediat.*, 8:452, 1936.
3. Sahyun, M.: *Am. J. Dig. Dis.*, 13:59, 1946.

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